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Pimentel, J.

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PTO-1590 (9-90)

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     FILE 'REGISTRY' ENTERED AT 11:51:03 ON 10 FEB 2000
                E LIPASE/CN
L1           132 S LIPASE ?/CN

     FILE 'CAPLUS' ENTERED AT 11:51:27 ON 10 FEB 2000
L1           132 SEA FILE=REGISTRY ABB=ON  PLU=ON  LIPASE ?/CN
L2           337 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOSOM?(S)(IMMUNOGLOBULI
                 N OR IMMUNO GLOBULIN OR IG)
L3             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 AND (L1 OR LIPASE OR
                 ANTILIPASE)

L1           132 SEA FILE=REGISTRY ABB=ON  PLU=ON  LIPASE ?/CN
L8           158 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOSOM? AND (L1 OR
                 LIPASE OR ANTILIPASE)
L9             7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (MAMMAL? OR AVES
                 OR BIRD OR AVIAN)

=> s l3 or l9

L10            8 L3 OR L9

=> d 1-8 .bevstr

L10  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         1999:64709  CAPLUS
DOCUMENT NUMBER:          130:138298
TITLE:                    Decreased fat absorption with an anti-
                        lipase antibody
INVENTOR(S):              Pimentel, Julio L.
PATENT ASSIGNEE(S):       Ximed Group Plc, UK
SOURCE:                   PCT Int. Appl., 18 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 9902187         A1   19990121      WO 1998-GB1998   19980706
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG,
             MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                          Searcher   :    Shears   308-4994
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AU 9882326 A1 19990208 AU 1998-82326 19980706
PRIORITY APPLN. INFO.: US 1997-888202 19970707
WO 1998-GB1998 19980706

AB A method for the decrease of fat absorption in any animal, wherein the animal is fed an antibody produced against **lipase**, an enzyme which is required for fat absorption. **Avian** egg-derived anti-**lipase** antibodies are disclosed for treating obesity in a **mammal** or an **avian**. Also, **avian** egg-derived antibodies (IgYs) against gastrointestinal enzyme such as amylase, trypsin, chymotrypsin, protease and other enzyme or antigen are used for reducing absorption of nutrients such as proteins, carbohydrates and lipids. These antibodies are mixed in food (concd., additive-added, refrigerated or frozen food) for human or animal consumption.

IT **9001-62-1, Lipase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**avian** egg-derived anti-**lipase** or anti-gastrointestinal enzyme antibodies are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:714487 CAPLUS
DOCUMENT NUMBER: 128:12135
TITLE: Guinea pig apolipoprotein C-II: expression in E. coli, functional studies of recombinant wild-type and mutated variants, and distribution on plasma lipoproteins
AUTHOR(S): Andersson, Yvonne; Lookene, Aivar; Shen, Yan; Nilsson, Solveig; Thelander, Lars; Olivecrona, Gunilla
CORPORATE SOURCE: Department of Medical Biochemistry and Biophysics, University of Umea, Umea, S-901 87, Swed.
SOURCE: J. Lipid Res. (1997), 38(10), 2111-2124
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Guinea pig apolipoprotein C-II (apoC-II) lacks four amino acid residues in the N-terminal, lipid-binding part compared to apoC-II from other **mammalian** species (Andersson, Y.; et al., 1991). To explore whether this structural difference explains the low ability of guinea pig plasma to activate lipoprotein **lipase** in vitro, we have expressed guinea pig apoC-II in Escherichia coli and have constructed an insertion mutant with the four missing amino acid residues compared to human apoC-II. With a synthetic emulsion of long-chain triacylglycerols, both the wild-type guinea pig apoC-II and the insertion mutant stimulated

lipoprotein **lipase** similar to human apoC-II, but with chylomicrons from an apoC-II-deficient patient, 5-10-fold more of both wild-type guinea pig apoC-II and the insertion mutant were needed. Studies of tryptophan fluorescence indicated a slight difference in how guinea pig apoC-II interacted with **liposomes**, and presumably with lipoproteins, as compared to human apoC-II. The level of apoC-II (11.5 .mu.g/mL) was lower in guinea pig compared to human plasma, and most of guinea pig apoC-II was on HDL-like particles. These had decreased ability to donate apoC-II to lipid emulsions compared to human HDL. Some guinea pig apoC-II was assocd. with LDL which, as demonstrated by surface plasmon resonance, had higher affinity for lipoprotein **lipase** than human LDL, and inhibited rather than stimulated the **lipase** reaction in vitro. Thus, whereas guinea pig apoC-II is fully competent to stimulate lipoprotein **lipase** , the sum of several different factors explains the low ability of guinea pig plasma to accomplish stimulation.

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:354033 CAPLUS
DOCUMENT NUMBER: 126:334373
TITLE: Antiatherogenic **liposomal** compositions and methods of using them
INVENTOR(S): Williams, Kevin Jon
PATENT ASSIGNEE(S): Williams, Kevin Jon, USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713501	A1	19970417	WO 1996-US16388	19961011
W: AU, CA, CN, JP, MX, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2231547	AA	19970417	CA 1996-2231547	19961011
AU 9675956	A1	19970430	AU 1996-75956	19961011
EP 863748	A1	19980916	EP 1996-938625	19961011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1228018	A	19990908	CN 1996-198729	19961011
PRIORITY APPLN. INFO.:			US 1995-5090	19951011
			WO 1996-US16388	19961011

AB The present invention provides a **liposomal** compn., method of using a **liposomal** compn., and devices and modes of operation of the devices and of the compns., and kits related

thereto. The invention provides for the reverse transport of cholesterol from peripheral tissues to the liver in a warm blooded **mammal** while controlling plasma atherogenic lipoprotein concns., including LDL concns. The method and mode of operation of the devices includes the step of administering an effective amt. of a multiplicity of acceptors comprised of phospholipids substantially free of sterol. The method optionally includes the step of periodically assaying atherogenic lipoprotein concns. with an assay during the treatment period to assess atherogenic lipoprotein concns. and obtain an atherogenic lipoprotein profile, and adjusting the administration in response to said profile. The large **liposomes** are dimensioned larger than fenestrations of an endothelial layer lining hepatic sinusoids in the liver so that the **liposomes** are too large to readily penetrate the fenestrations of one variant. The therapeutically effective amts. are in the range of about 10 mg to about 1600 mg phospholipid per kg body wt. per dose. A pharmaceutical compn. and related kit for mobilizing peripheral cholesterol and sphingomyelin that enters the liver of a subject consisting essentially of **liposomes** of a size and shape larger than fenestrations of an endothelial layer lining hepatic sinusoids in the liver is also provided. The invention also provides for control of cholesterol related genes and other compds.

IT **9001-62-1, Lipase**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(assessment of activity of; antiatherogenic **liposomal** compns. and methods of using them)

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:18384 CAPLUS
DOCUMENT NUMBER: 126:43610
TITLE: Animal gene therapy expression cassettes and DNA constructs for treatment of infectious diseases
INVENTOR(S): Gagne, Marc
PATENT ASSIGNEE(S): Immunova, Can.; Gagne, Marc
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9635793	A1	19961114	WO 1996-CA297	19960510

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

CA 2220472	AA	19961114	CA 1996-2220472	19960510
AU 9656416	A1	19961129	AU 1996-56416	19960510
EP 828839	A1	19980318	EP 1996-913403	19960510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11505113	T2	19990518	JP 1996-533627	19960510
PRIORITY APPLN. INFO.:			GB 1995-9461	19950510
			WO 1996-CA297	19960510

AB The present invention relates to DNA sequences, expression cassettes and DNA constructs for use in therapy, specifically in gene therapy for the treatment of infectious diseases such as mastitis. Also included are pharmaceutical and veterinary compns. contg. the constructs, and cells which have been transformed with the DNA and which are suitable for implantation into a host **mammal**. The gene therapy of infectious diseases can be effected in situ in targeted tissue or systemically.

IT **9001-62-1P**, Triacylglycerol **lipase**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bile-salt-stimulated, therapeutic; animal gene therapy expression cassettes and DNA constructs for treatment of infectious diseases)

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:577654 CAPLUS
DOCUMENT NUMBER: 125:214231
TITLE: Direct gene transfer into the mammary gland of immature ruminants by infusion
INVENTOR(S): Karatzas, Constantinos; Lazaris-Karatzas, Anthoula; Turner, Jeffrey Donald
PATENT ASSIGNEE(S): Nexia Biotechnologies, Inc., Can.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622379	A2	19960725	WO 1996-CA29	19960119
WO 9622379	A3	19961107		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN

US 5780009	A	19980714	US 1995-377016	19950120
CA 2210897	AA	19960725	CA 1996-2210897	19960119
AU 9644284	A1	19960807	AU 1996-44284	19960119
EP 805869	A2	19971112	EP 1996-900484	19960119

R: BE, DE, FR, GB, NL

PRIORITY APPLN. INFO.:	US 1995-377016	19950120
	WO 1996-CA29	19960119

AB A method for expressing a heterologous gene in the mammary gland of a ruminant is described. The invention is useful for producing a heterologous protein(s) in the milk of the **mammal**, for producing a heterologous enzyme(s) which is tethered to the mammary epithelial cell membrane and which can act on a component of the milk of the **mammal**, and for providing an antisense oligonucleotide(s) or ribozyme(s) which inhibits expression of a gene to a mammary epithelial cell. The method involves infusing a liq. complex including a genetic construct into a ductal tree of the **mammal**. The liq. complex can be infused before the **mammal** reaches sexual maturity and after the **mammal** develops a functional streak canal. Alternatively, a liq. complex that is free of live retroviruses can be infused. If desired, the infused genetic construct can be treated with a polycationic compd. and/or a lipid to improve the efficiency with which it is taken up by an epithelial cell of the mammary gland. Successful expression of genes for human growth hormone (yield 1-2.5 ng/mL milk) and tissue plasminogen activator using a constitutive cytomegalovirus promoter is demonstrated. Optimization of **liposome** -mediated transformation is described.

IT **9001-62-1P, Lipase**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(gene for, expression in mammary gland of; direct gene transfer into mammary gland of immature ruminants by infusion into ductal tree)

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:	1993:250615 CAPLUS
DOCUMENT NUMBER:	118:250615
TITLE:	Chymotryptic cleavage of lipoprotein **lipase**. Identification of cleavage sites and functional studies of the truncated molecule
AUTHOR(S):	Lookene, Aivar; Bengtsson-Olivecrona, Gunilla
CORPORATE SOURCE:	Dep. Med. Biochem. Biophys., Univ. Umea, Umea, S-901 87, Swed.
SOURCE:	Eur. J. Biochem. (1993), 213(1), 185-94 CODEN: EJBCAI; ISSN: 0014-2956

Searcher : Shears 308-4994

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of bovine lipoprotein **lipase** (LPL) with chymotrypsin results in cleavage between residues Phe390-Ser391 and between Trp392-Ser393, indicating that this region is exposed in the native conformation of LPL. Two main fragments are generated, one large including the amino-terminus (chymotrypsin-truncated LPL = c-LPL) and one small, carboxy-terminal fragment. The small fragment is not stable, but is further degraded by the protease. Isolated c-LPL has full catalytic activity against tributyryl glycerol (tributyrin) and p-nitrophenyl butyrate, while the activity against emulsions of long-chain triacylglycerols and against **liposomes** is reduced and the activity against milk fat globules and chylomicrons is lost. Several properties of c-LPL were investigated. It was found that c-LPL interacts with apolipoprotein CII (apo CII) as efficiently as intact LPL. The truncated enzyme bound to **liposomes** and to emulsions of long-chain triacylglycerols as well as the intact enzyme did. In contrast, c-LPL did not bind to milk fat globules or to chylomicrons. The activity of c-LPL was more sensitive to inhibition by other lipid-binding proteins, e.g. apolipoprotein CIII (apo CIII), than was the intact enzyme. The affinity for heparin was as high with c-LPL as with intact LPL. Like intact LPL, c-LPL is dimeric in its active form, as evidenced by sucrose d. gradient centrifugation. It is concluded that the reduced catalytic and lipid-binding properties of c-LPL compared with intact LPL are related to the properties of the substrate interface. It is speculated that the carboxy-terminal part of LPL contains a secondary lipid-binding site, which is important for activity against chylomicrons and related substrates.

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:55628 CAPLUS
DOCUMENT NUMBER: 118:55628
TITLE: Antigen determination by liposome enzyme immunoassay
INVENTOR(S): Kotani, Kiyoshi
PATENT ASSIGNEE(S): Toyo Ink Mfg. Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04303770	A2	19921027	JP 1991-93145	19910330

AB A procedure for antigen (e.g. IgG) detn. by liposome enzyme immunoassay involves: adsorbing test antigen on a 1st antibody (e.g.

goat anti-mouse IgG antibody)-sensitized microplate, washing, incubating with marker (e.g. horseradish peroxide)-contg. 2nd antibody-sensitized liposomes, again washing, treating with phospholipase A2 to release the peroxidase content, and spectrometrically detg. the enzyme activity. The method detects antigen concns. in the range of pmol-fmol and is more sensitive than conventional sandwich EIA.

IT **9001-62-1, Lipase**
RL: ANST (Analytical study)
(in antigen detn. by liposome EIA with enzyme-contg. sensitized liposomes)

L10 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:557510 CAPLUS
DOCUMENT NUMBER: 117:157510
TITLE: Amphotericin B-phospholipid interactions responsible for reduced **mammalian** cell toxicity
AUTHOR(S): Perkins, Walter R.; Minchey, Sharma R.; Boni, Lawrence T.; Swenson, Christine E.; Popescu, Mircea C.; Pasternack, Robert F.; Janoff, Andrew S.
CORPORATE SOURCE: Liposome Co. Inc., Princeton, NJ, 08540, USA
SOURCE: Biochim. Biophys. Acta (1992), 1107(2), 271-82
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB When interacting with phospholipid in an aq. environment, amphotericin B forms unusual structures of markedly reduced toxicity (Janoff et al., 1988). These structures, which appear ribbon-like by freeze-fracture electron microscopy (EM), are found exclusively at amphotericin B to lipid mole ratios of 1:3 to 1:1. At lower mole ratios they occur in combination with **liposomes**. CD spectra revealed 2 distinct modes of lipid-amphotericin B interaction, one for **liposomes** and one for the ribbon-like structures. In isolated **liposomes**, amphotericin B which comprised 3-4 mol percent of the bulk lipid was monomeric and exhibited a hemolytic activity comparable to amphotericin B suspended in deoxycholate. Above 3-4 mol% amphotericin B, ribbon-like structures emerged and CD spectra indicated drug-lipid complexation. Minimal inhibitory concns. for Candida albicans of **liposomal** and complexed amphotericin B were comparable and could be attributed to amphotericin release as a result of lipid breakdown within the ribbon-like material by a heat labile extracellular yeast product (**lipase**). Neg. stain EM of the ribbon-like structures indicated that the ribbon-like appearance seen by freeze-fracture EM arises as a consequence of the cross-fracturing of what are aggregated, collapsed single lamellar, presumably interdigitated, membranes. Studies examg. complexation

of amphotericin B with either DMPC or DMPG demonstrated that headgroup interactions played little role in the formation of the ribbon-like structures. With these results it is proposed that ribbon-like structures result from phase sepn. of amphotericin B-phospholipid complexes within the phospholipid matrix such that amphotericin B release, and thus acute toxicity, is curtailed. Formation of amphotericin B-lipid structures such as those described here indicates a possible new role for lipid as a stabilizing matrix for drug delivery of lipophilic substances, specifically where a highly ordered packing arrangement between lipid and compd. can be achieved.

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, CABA, AGRICOLA, FSTA' ENTERED AT 12:00:38 ON 10 FEB 2000)

L11 41 S L10
L12 33 DUP REM L11 (8 DUPLICATES REMOVED)

L12 ANSWER 1 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:481981 BIOSIS
DOCUMENT NUMBER: PREV199900481981
TITLE: Differential binding of triglyceride-rich lipoproteins to lipoprotein **lipase**.
AUTHOR(S): Xiang, Shi-Qin; Cianflone, Katherine; Kalant, David; Sniderman, Allan D. (1)
CORPORATE SOURCE: (1) Mike Rosenbloom Laboratory for Cardiovascular Research, McGill University Health Center, Montreal, PQ, H3A 1A1 Canada
SOURCE: Journal of Lipid Research, (Sept., 1999) Vol. 40, No. 9, pp. 1655-1662.
ISSN: 0022-2275.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In comparison to very low density lipoprotein (VLDL), chylomicrons are cleared quickly from plasma. However, small changes in fasting plasma VLDL concentration substantially delay postprandial chylomicron triglyceride clearance. We hypothesized that differential binding to lipoprotein **lipase** (LPL), the first step in the lipolytic pathway, might explain these otherwise paradoxical relationships. Competition binding assays of different lipoproteins were performed in a solid phase assay with purified bovine LPL at 4degreeC. The results showed that chylomicrons, VLDL, and low density lipoprotein (LDL) were able to inhibit specific binding of 125I-labeled VLDL to the same extent (85.1% +- 13.1, 100% +- 6.8, 90.7% +- 23.2% inhibition, P = NS), but with markedly different efficiencies. The rank order of inhibition (Ki) was chylomicrons (0.27 +- 0.02 nM apoB) > VLDL (12.6 +- 3.11 nM apoB) > LDL (34.8 +- 11.1 nM apoB). By contrast, neither triglyceride (TG)

liposomes, high density lipoprotein(HDL), nor LDL from patients with familial hypercholesterolemia were efficient at displacing the specific binding of 125I-labeled VLDL to LPL (30%, 39%, and no displacement, respectively). Importantly, smaller hydrolyzed chylomicrons had less affinity than the larger chylomicrons (Ki = 2.34 +- 0.85 nM vs. 0.27 +- 0.02 nM apoB respectively, P < 0.01). This was also true for hydrolyzed VLDL, although to a lesser extent. Chylomicrons from patients with LPL deficiency and VLDL from hypertriglyceridemic subjects were also studied. Taken together, our results indicate an inverse linear relationship between chylomicron size and Ki whereas none was present for VLDL. We hypothesize that the differences in binding affinity demonstrated in vitro when considered with the differences in particle number observed in vivo may largely explain the paradoxes we set out to study.

L12 ANSWER 2 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:183543 BIOSIS
DOCUMENT NUMBER: PREV199900183543
TITLE: Lysine 49 phospholipase A2 proteins.
AUTHOR(S): Ownby, Charlotte L. (1); Selistre de Araujo, Heloisa S.; White, Steven P.; Fletcher, Jeffrey E.
CORPORATE SOURCE: (1) Department of Anatomy, Pathology and Pharmacology, Oklahoma State University, Stillwater, OK, 74078-0350 USA
SOURCE: Toxicon, (March, 1999) Vol. 37, No. 3, pp. 411-445. ISSN: 0041-0101.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB The structures of several K49 PLA2 proteins have been determined and these differ as a group in several regions from the closely related D49 PLA2 enzymes. One outstanding difference is the presence of a high number of positively charged residues in the C-terminal region which combined with the overall high number of conserved lysine residues gives the molecule an interfacial adsorption surface which is highly positively charged compared to the opposite surface of the molecule. Although some nucleotide sequences have been reported, progress in obtaining active recombinant proteins has been slow. The K49 proteins exert several toxic activities, including myotoxicity, anticoagulation and edema formation. The most studied of these activities is myotoxicity. The myotoxicity induced by the K49 PLA2 proteins is histologically similar to that caused by the D49 PLA2 myotoxins, with some muscle fiber types possibly more sensitive than others. Whereas it is clear that the K49 PLA2 myotoxins lyse the plasma membrane of the affected muscle cell in vivo, the exact mechanism of this lysis is not known. Also, it is not known whether the toxin is internalized before, during or after the initial lysis or ever. The K49 PLA2 toxins lyse **liposomes** and cells in culture and in the latter, the PLA2 myotoxins exert at least two

distinct mechanisms of action, neither of which is well-characterized. While the K49 PLA2 proteins are enzymatically inactive on artificial substrates, the toxins cause fatty acid production in cell cultures. Whether the fatty acid release is due to the enzymatic activity of the K49 PLA2 or stimulation of tissue **lipases**, is unknown. While there may be a role for fatty acid production in one mechanism of myotoxicity, a second mechanism appears to be independent of enzymatic activity. Although we are beginning to understand more about the structure of these toxins, we still know little about the precise mechanism by which they interact with the skeletal muscle cell in vivo.

L12 ANSWER 3 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:402059 BIOSIS
DOCUMENT NUMBER: PREV199800402059
TITLE: Interaction between ApoB and hepatic **lipase** mediates the uptake of ApoB-containing lipoproteins.
AUTHOR(S): Choi, Sungshin Y. (1); Goldberg, Ira J.; Curtiss, Linda K.; Cooper, Allen D.
CORPORATE SOURCE: (1) Research Inst., Palo Alto Med. Foundation, 860 Bryant St., Palo Alto, CA 94301 USA
SOURCE: Journal of Biological Chemistry, (Aug. 7, 1998) Vol. 273, No. 32, pp. 20456-20462.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Hepatic **lipase** (HL) on the surface of hepatocytes and endothelial cells lining hepatic sinusoids, the adrenal glands, and the ovary hydrolyzes triglycerides and phospholipids of circulating lipoproteins. Its expression significantly enhances low density lipoprotein (LDL) uptake via the LDL receptor pathway. A specific interaction between LPL, a homologous molecule to HL, and apoB has been described (Choi, S. Y., Sivaram, P., Walker, D. E., Curtiss, L. K., Gretch, D. G., Sturley, S. L., Attie, A. D., Deckelbaum, R. J., and Goldberg, I. J. (1995) J. Biol. Chem. 270, 8081-8086). The present studies tested the hypothesis that HL enhances the uptake of lipoproteins by a specific interaction of HL with apoB. On a ligand blot, HL bound to apoB26, 48, and 100 but not to apoE or apoAI. HL binding to LDL in a plate assay with LDL-coated plates was significantly greater than to bovine serum albumin-coated plates. Neither heat denatured HL nor bacterial fusion protein of HL bound to LDL in the plate assays. 125I-LDL bound to HL-saturated heparin-agarose gel with a Kd of 52 nM, and somewhat surprisingly, this binding was not inhibited by excess LPL. In cell culture experiments HL enhanced the uptake of 125I-LDL at both 4 and 37degreeC. The enhanced binding and uptake of LDL was significantly inhibited by monoclonal anti-apoB antibodies. In contrast to LPL, both amino- and carboxyl-terminal antibodies blocked the apoB interaction with HL to the same extent. Thus, we conclude that there

is a unique interaction between HL and apoB that facilitates the uptake of apoB-containing lipoproteins by cells where HL is present.

L12 ANSWER 4 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:207976 BIOSIS
DOCUMENT NUMBER: PREV199800207976
TITLE: Metabolic fate of exogenous diacylglycerols in A10 smooth muscle cells.
AUTHOR(S): Chuang, Mariette; Severson, David L. (1)
CORPORATE SOURCE: (1) Smooth Muscle Res. Group, Fac. Med., Univ. Calgary, 3330 Hospital Drive N.W., Calgary, AB T2N 4N1 Canada
SOURCE: Biochimica et Biophysica Acta, (Feb. 16, 1998) Vol. 1390, No. 2, pp. 149-159.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The metabolic fate of exogenous diacylglycerols, 1-palmitoyl-2-(1-14C)oleoyl-sn-glycerol (2-(14C)POG) and 1-stearoyl-2-(1-14C)arachidonoyl-sn-glycerol (2-(14C)SAG), was determined after incubation of A10 smooth muscle cells with **liposomal** suspensions. Hydrolysis through a diacylglycerol (DG) **lipase** pathway was the predominant metabolic fate; more than 80% of cell-associated radioactivity from 2-(14C)POG and 2-(14C)SAG was recovered in lipolytic products, monoacyl- glycerol (MG) and fatty acids (FA), which were present in the incubation medium. Hydrolysis of 2-(14C)POG was reduced completely by tetrahydrolipstatin, a **lipase** inhibitor. Very little radioactivity from either 2-(14C)POG or 2-(14C)SAG was incorporated into triacylglycerol or phospholipids. DG **lipase** and kinase activities were measured by in vitro enzyme assays. 1-(1-14C)Palmitoyl-2-oleoyl-sn-glycerol (1-(14C)POG) was phosphorylated (kinase activity) to a greater extent than 2-(14C)SAG in assays with both soluble and particulate subcellular fractions from A10 cells. DG **lipase** activity (hydrolysis of 1-(14C)POG and 2-(14C)SAG) was markedly stimulated by the addition of 20 mM MgCl2 and 20 mM ATP to the assay. Under optimal assay conditions, DG **lipase** activity exhibited little substrate specificity. Our findings indicate that exogenous DG are mainly hydrolyzed by DG and MG **lipases** in A10 smooth muscle cells; as a result, signalling mechanisms responding to DG second messengers will be attenuated.

L12 ANSWER 5 OF 33 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998040289 MEDLINE
DOCUMENT NUMBER: 98040289
TITLE: Guinea pig apolipoprotein C-II: expression in E. coli, functional studies of recombinant wild-type and mutated variants, and distribution on plasma

lipoproteins.

AUTHOR: Andersson Y; Lookene A; Shen Y; Nilsson S; Thelander L; Olivecrona G

CORPORATE SOURCE: Department of Medical Biochemistry and Biophysics, University of Umea, Sweden.

SOURCE: JOURNAL OF LIPID RESEARCH, (1997 Oct) 38 (10) 2111-24.
Journal code: IX3. ISSN: 0022-2275.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199803

ENTRY WEEK: 19980304

AB Guinea pig apolipoprotein C-II (apoC-II) lacks four amino acid residues in the amino-terminal, lipid-binding part compared to apoC-II from other **mammalian** species (Andersson et al. 1991. J. Biol. Chem. 266: 4074-4080). To explore whether this structural difference explains the low ability of guinea pig plasma to activate lipoprotein **lipase** in vitro, we have expressed guinea pig apoC-II in Escherichia coli and have constructed an insertion mutant with the four missing amino acid residues compared to human apoC-II. With a synthetic emulsion of long-chain triacylglycerols, both the wild-type guinea pig apoC-II and the insertion mutant stimulated lipoprotein **lipase** similar to human apoC-II, but with chylomicrons from an apoC-II-deficient patient, 5- to 10-fold more of both wild-type guinea pig apoC-II and the insertion mutant were needed. Studies of tryptophane fluorescence indicated a slight difference in how guinea pig apoC-II interacted with **liposomes**, and presumably with lipoproteins, as compared to human apoC-II. The level of apoC-II (11.5 +/- 5.4 microg/ml) was lower in guinea pig compared to human plasma, and most of guinea pig apoC-II was on HDL-like particles. These had decreased ability to donate apoC-II to lipid emulsions compared to human HDL. Some guinea pig apoC-II was associated with LDL which, as demonstrated by surface plasmon resonance, had higher affinity for lipoprotein **lipase** than human LDL, and inhibited rather than stimulated the **lipase** reaction in vitro. We conclude that while guinea pig apoC-II is fully competent to stimulate lipoprotein **lipase**, the sum of several different factors explains the low ability of guinea pig plasma to accomplish stimulation.

L12 ANSWER 6 OF 33 SCISEARCH COPYRIGHT 2000 ISI (R)

ACCESSION NUMBER: 97:770748 SCISEARCH

THE GENUINE ARTICLE: YA808

TITLE: Amphotericin B lipid complex

AUTHOR: Rapp R P (Reprint); Gubbins P O; Evans M E

CORPORATE SOURCE: UNIV KENTUCKY, COLL PHARM, MED CTR, LEXINGTON, KY

40536 (Reprint); UNIV ARKANSAS MED SCI, COLL PHARM, LITTLE ROCK, AR 72205; UNIV KENTUCKY, COLL MED, MED CTR, LEXINGTON, KY 40536
COUNTRY OF AUTHOR: USA
SOURCE: ANNALS OF PHARMACOTHERAPY, (OCT 1997) Vol. 31, No. 10, pp. 1174-1186.
Publisher: HARVEY WHITNEY BOOKS CO, PO BOX 42696, CINCINNATI, OH 45242.
ISSN: 1060-0280.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 67

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB OBJECTIVE: To evaluate the published data on the effectiveness and safety of amphotericin B lipid complex (ABLC) for the treatment of invasive mycosis and to evaluate data describing the pharmacologic properties and pharmacokinetic behavior of ABLC in both animals and humans.

DATA SOURCE: A MEDLINE search was conducted to identify literature published from 1965 to January 1997 for amphotericin B deoxycholate (DCAB) and ABLC. In addition, preliminary data published as abstracts and presented al national conferences on infectious disease and hematology within the last 6 years were also included in this review.

STUDY SELECTION: Both human and animal studies were reviewed. Animal and in vitro studies were selected to evaluate the pharmacologic and toxicologic properties of ABLC. For the evaluation of the efficacy, safety, and pharmacokinetic behavior of ABLC, large, well-controlled studies were reviewed, In addition, data from open-label and emergency use protocols were also included in the review,

DATA EXTRACTION: The study and analytical methods, results, and conclusions of the selected studies were evaluated. Pharmacokinetic data for both ABLC and DCAB that were derived from human subjects were also evaluated.

DATA SYNTHESIS: DCAB has been the cornerstone for the treatment of invasive mycosis, even though it has a narrow therapeutic index Infusion-related toxicities (e.g., fever, chills. rigors) are likely due to DCAB stimulation of cytokine and prostaglandin synthesis, Conversely, nephrotoxicity, the primary non-infusion-related toxicity, likely results from the nonselective cytotoxic interaction between DCAB and cholesterol-containing **mammalian** cells, ABLC represents a new approach to improving the therapeutic index of DCAB. **Mammalian** cytotoxicity is attenuated by complexing amphotericin B to a mixture of phospholipids. This alters the affinity of amphotericin B and decreases its selective transfer from the complex to cholesterol-containing **mammalian** cells, Fungi also possess **Lipase**, which improves the selective

transfer from the complex to ergosterol-containing cell membranes, In humans, the lipid formulation increases the volume of distribution of amphotericin B. Thus, compared with DCAB, larger doses of ABLC can be administered for a longer duration with less nephrotoxicity. However, the prevalence of infusion-related toxicities associated with ABLC is similar to that of DCAB, Whether the alteration in distribution improves efficacy by improving tissue concentrations of amphotericin B has not been determined. The cost of this agent will limit its use.

CONCLUSIONS: ABLC has been shown to be at least as effective as DCAB, and it has been well tolerated in the clinical studies to date. Despite large dosages and extended courses of administration, there is little nephrotoxicity associated with its use, However, the cost of this agent will limit its use to the treatment of refractory mycosis or to cases where DCAB is contraindicated due to significant renal insufficiency.

L12 ANSWER 7 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:139943 BIOSIS
DOCUMENT NUMBER: PREV199799439146
TITLE: Tissue specific overexpression of hormone sensitive **lipase** in adipose tissue mediated by gene therapy.
AUTHOR(S): Makovsky, N. J.; Schlaepfer, I. R.; Eckel, R. H.
CORPORATE SOURCE: Dep. Med., Univ. Colorado Health Sci. Cent., Denver, CO USA
SOURCE: Journal of Investigative Medicine, (1997) Vol. 45, No. 1, pp. 141A.
Meeting Info.: Meeting of the American Federation for Medical Research, Western Regional Carmel, California, USA February 5-8, 1997
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L12 ANSWER 8 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:238816 BIOSIS
DOCUMENT NUMBER: PREV199799538019
TITLE: Extracellular **lipases** of the plantar human stratum corneum.
AUTHOR(S): Zellmer, Sebastian; Koelsch, Regine; Lasch, Juergen
CORPORATE SOURCE: Inst. Physiol. Chem., Martin-Luther-Univ. Halle-Wittenberg, D-06097 Halle Germany
SOURCE: European Journal of Cell Biology, (1997) Vol. 72, No. SUPPL. 43, pp. 57.
Meeting Info.: Annual Meeting of the Deutsche Gesellschaft fuer Zellbiologie (German Society for Cell Biology) Halle, Germany March 16-20, 1997
ISSN: 0171-9335.

DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L12 ANSWER 9 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:103118 BIOSIS
DOCUMENT NUMBER: PREV199698675253
TITLE: Oxidation of low density lipoproteins greatly enhances their association with lipoprotein **lipase** anchored to endothelial cell matrix.
AUTHOR(S): Auerbach, Bruce J. (1); Bisgaier, Charles L.; Wolle, Joachim; Saxena, Uday
CORPORATE SOURCE: (1) Atherosclerosis Therapeutics, Parke-Davis Pharmaceutical Res., Div. Warner-Lambert Co., 2800 Plymouth Road, Ann Arbor, MI 48105 USA
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 3, pp. 1329-1335.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Native and oxidized low density lipoprotein retention within arterial wall endothelial cell matrix (ECM) is an early event in the pathogenesis of atherosclerosis. Previously we showed lipoprotein **lipase** (LPL) addition to ECM enhanced the retention of apoB-containing lipoproteins. In the present studies we examined whether the oxidation of low density lipoprotein (LDL) increases its retention by LPL-containing ECM. Except where noted, 125I-labeled moderately oxidized LDL (ModOxLDL) was prepared by long term storage of 125I-LDL. Without LPL, 125I-ModOxLDL matrix binding was low and nonsaturable. LPL preanchored to ECM resulted in 125I-ModOxLDL binding that was saturable and 20-fold greater than in the absence of LPL, with an association constant equal to 2.6 nM. Copper-oxidized LDL (Cu-OxLDL) was able to compete with 125I-ModOxLDL, whereas a 60-fold native LDL excess had no effect. Reconstituted apolipoprotein B from Cu-OxLDL also reduced 125I-ModOxLDL to LPL, whereas **liposomes** derived from the lipid extract of Cu-OxLDL had no effect on binding. These data suggest that the increased binding of oxidized LDL to LPL-ECM may be due to the exposure of novel apoB binding sites and not an oxidized lipid moiety. 125I-ModOxLDL binding was also not affected by either preincubation with a 300-fold molar excess of apoE-poor HDL or an 340-fold molar excess of Cu-OxHDL. In contrast, a 4-fold apoE-rich HDL excess (based on protein) totally inhibited 125I-ModOxLDL matrix retention. Positively charged peptides of polyarginine mimicked the effect of apoE-rich HDL in reducing the 125I-ModOxLDL retention; however, polylysine had no effect. We postulate that the oxidation of LDL may be a mechanism that enhances LDL retention by the ECM-bound LPL and that the protective effects of apoE-containing HDL may in part be due to its ability to block the retention of oxidized LDL in vivo.

L12 ANSWER 10 OF 33 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 960989535 JICST-EPlus
TITLE: Research on invention, improvement and modification of medical materials with high functions and on peripheral technology. Research on design of drug carrier by lipid minuteness disperse system and on its evaluation method. (Human Science Promotion Foundation S)
AUTHOR: OKADA SATOSHI
CORPORATE SOURCE: National Inst. of Hygienic Sciences
SOURCE: Kanmin Kyodo Purojekuto Kenkyu Hokoku. Heisei 7 Nendo. Dai4 Bun'ya. Iryo, Fukushi Sabisu no Kiso to shiteno Iyo Zairyo no Hyoka, Kairyo, Kaihatsu Gijutsu no Kenkyu, (1996) pp. 85-94. Journal Code: N19962649 (Fig. 8, Tbl. 2, Ref. 9)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

L12 ANSWER 11 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:546147 BIOSIS
DOCUMENT NUMBER: PREV199698560447
TITLE: Human Hepatic and Lipoprotein **Lipase**: The Loop Covering the Catalytic Site Mediates **Lipase** Substrate Specificity.
AUTHOR(S): Dugi, Klaus A.; Dichek, Helen L.; Santamarina-Fojo, Silvia (1)
CORPORATE SOURCE: (1) Mol. Dis. Branch, NHLBI, NIH, Build. 10, Room 7N115, 9000 Rockville Pike, Bethesda, MD 20892 USA
SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 43, pp. 25396-25401.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Hepatic **lipase** (HL) and lipoprotein **lipase** (LPL) are key enzymes that mediate the hydrolysis of triglycerides (TG) and phospholipids (PL) present in circulating plasma lipoproteins. Relative to triacylglycerol hydrolysis, HL displays higher phospholipase activity than LPL. The structural basis for this difference in substrate specificity has not been definitively established. We recently demonstrated that the 22-amino acid loops ("lids") covering the catalytic sites of LPL and HL are critical for the interaction with lipid substrate (Dugi, K. A., Dichek, H. L., Talley, G. D., Brewer, H. B., Jr., and Santamarina-Fojo, S. (1992) J. Biol. Chem. 267, 25086-25091). To determine whether the **lipase** lid plays a role in conferring the different substrate specificities of HL and LPL, we have generated four

chimeric **lipases**. Characterization of these chimeric enzymes using TG (triolein and tributyrin) or PL (dioleoylphosphatidylcholine (DOPC) vesicles, DOPC proteoliposomes, and DOPC-mixed **liposomes**) substrates demonstrated marked differences between their relative PL/TG hydrolyzing activities. Chimeric LPL containing the lid of HL had reduced triolein hydrolyzing activity (49% of the wild type), but increased phospholipase activity in DOPC vesicle, DOPC proteoliposome, and DOPC-mixed **liposome** assay systems (443, 628, and 327% of wild-type LPL, respectively). In contrast, chimeric HL containing the LPL lid was more active against triolein (123% of the wild type) and less active against DOPC (23, 0, and 30%, respectively) than normal HL. Similar results were obtained when the **lipase** lids were exchanged in chimeric enzymes containing the NH-2-terminal end of LPL and the COOH-terminal domain of HL. Exchange of the LPL and HL lids resulted in a reversal of the phospholipase/neutral **lipase** ratio, establishing the important role of this region in mediating substrate specificity. In summary, the lid covering the catalytic domains in LPL and HL plays a crucial role in determining **lipase** substrate specificity. The lid of LPL confers preferential triglyceride hydrolysis, whereas the lid of HL augments phospholipase activity. This study provides new insight into the structural basis for the observed in vivo differences in LPL and HL function.

L12 ANSWER 12 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:440166 BIOSIS
DOCUMENT NUMBER: PREV199497453166
TITLE: Transient changes in the mononuclear phagocyte system following administration of the blood substitute **liposome**-encapsulated haemoglobin.
AUTHOR(S): Rudolph, Alan S. (1); Cliff, Richard O.; Spargo, Barry J.; Spielberg, Helmut
CORPORATE SOURCE: (1) Cent. Biomolecular Sci. Eng., Code 6900, Naval Res. Lab., Washington, DC 20375-5348 USA
SOURCE: Biomaterials, (1994) Vol. 15, No. 10, pp. 796-804. ISSN: 0142-9612.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We have examined the effects of administration of the blood substitute, **liposome**-encapsulated haemoglobin (LEH), in the normovolaemic rat. Test groups included LEH, lyophilized EH, the **liposome** vehicle, unencapsulated haemoglobin and normal saline, which were injected into the tail vein (n = 6; n = 3 for sham and saline groups). Administration of LEH (2.5 g phospholipid, 1.25 g haemoglobin/kg rat) was followed by blood sampling at 2 h, 24 h, 1 wk and 2 wk. Blood samples were analysed for alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyltransferase, total and indirect bilirubin, serum

creatinine, albumin, total protein, **lipase**, cholesterol, blood urea nitrogen, hematocrit, haemoglobin and differential white blood cell counts. Observed effects following injection were mild and transient, with baseline values recovered at 1 wk. Alanine aminotransferase increased moderately in the LEH group at 24 h to 601 +- 143 IU/dl (P lt 0.0001), with a return to baseline at 1 wk. Aspartate aminotransferase showed a smaller increase from 46 +- 5 to 162 +- 40 at 24 h and also returned to baseline at the 1 wk measurement (P lt 0.001). The transient increase in serum transaminases was not observed for the lyophilized LEH group. Tissue sections showed accumulation of **liposome** groups in resident macrophages of the liver and spleen. Incubation of an adherent population of human peripheral blood monocytes with LEH in culture did not elicit the production of the inflammatory cytokine, tumour necrosis factor. Pre-incubation of monocytes with LEH prior to exposure to endotoxin did, however, result in a reduced expression of this inflammatory cytokine.

L12 ANSWER 13 OF 33 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 940969107 JICST-EPlus
TITLE: Effect of particle size on plasma clearance of lipid microsphere in rats.
AUTHOR: IMAEDA NORISHIGE; MATSUDA HIROSHI; TSUDA YOSHIO; UEDA YASUO; YOKOYAMA KAZUMASA
CORPORATE SOURCE: Green Cross Corp., Central Res. Lab.
SOURCE: Drug Deliv Syst, (1994) vol. 9, no. 5, pp. 339-344. Journal Code: X0225A (Fig. 3, Tbl. 1, Ref. 12) CODEN: DDSYEI; ISSN: 0913-5006
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB The double-labeled lipid microspheres with 3H-dipalmitoylphosphatidylcholine(DPPC) and 14C-tripalmitin(TP) having various particle sizes: small; 50nm, medium; 130nm, large; 215nm in mean diameters, were prepared by a Microfluidics homogenizer. After intravenous administration of microspheres to rats, plasma levels of radioactivities were measured from 1 to 360min periodically. The smaller the particle size of lipid microsphere was, the faster the elimination of radioactivities from plasma was; which was contrary to the results of **liposomes**. Elimination of 14C-TP from plasma was faster than that of 3H-DPPC in any microspheres, particularly in small and medium microspheres. This result suggested that triglyceride in microsphere core was hydrolysed and eliminated from circulation, while phospholipid was remained in the surface lipid monolayer of microsphere. Sucrose step-density gradient fractionation of the rat plasma samples showed that a large part of the radioactivity moved to the high-density fraction from the low-density (microshere's) fraction. The transported radioactivity

of 14C was much in the smaller microsheres. These results suggested that clearance of microsphere from plasma was much influenced by the interaction with apoproteins and **lipases** rather than the uptake by reticuloendotherial system. A part of this work was supported by a grant from Human Science Foundation. (author abst.)

L12 ANSWER 14 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:342884 BIOSIS
DOCUMENT NUMBER: PREV199497355884
TITLE: Murine macrophages secrete factors that enhance uptake of non-lipoprotein (3H)cholesteryl ester by aortic smooth muscle cells.
AUTHOR(S): Stein, O.; Ben-Naim, M.; Dabach, Y.; Hollander, G.; Stein, Y. (1)
CORPORATE SOURCE: (1) Lipid Res. Lab., Dep. Med., Hadassah Univ. Hosp., P.O. Box 12 220, Jerusalem 91120 Israel
SOURCE: Biochimica et Biophysica Acta, (1994) Vol. 1212, No. 3, pp. 305-310.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We have recently demonstrated that macrophage conditioned medium (MP medium) and beta-VLDL enhance cholesterol esterification in cultured aortic smooth muscle cells by LDL receptor mediated and other pathways (Stein, O. et al. (1993) Arteroscl. Thromb. 13, 1350-1358). In view of the presence of extracellular non-lipoprotein cholesteryl ester (in the form of lipid droplets) in the atheroma, the effect of MP medium on the cellular uptake of **liposomal** cholesteryl linoleyl ether (CLE) or cholesteryl ester (CE) was studied. After 4 h incubation in MP medium, the uptake of **liposomal** (3H)CLE was up to 10-fold higher than in the presence of control medium of the same composition but not conditioned with macrophages (DV medium). Similar results were seen also with HSF derived from LDL receptor negative donors. The MP medium-stimulated uptake of **liposomal** (3H)CE resulted also in hydrolysis of 70-90% of the labeled compound, indicating that the (3H)CE was intracellular. While the MP medium effect on **liposomal** (3H)CLE uptake was evident after 4 h, its effect on (3H)cholesterol esterification by SMC in the presence of beta-VLDL could be demonstrated only after 24 h. Addition of apoE to MP medium resulted in a small (30-40%) increase in the uptake of **liposomal** (3H)CLE; however, it was augmented more than 4-fold when apoE was added to DV medium. The MP medium effect on the uptake of **liposomal** (3H)CLE was interfered with by heparin, anti-LPL antibody or heparinase, while these treatments did not affect (3H)cholesterol esterification in the presence of beta-VLDL. These results suggest that the interaction between SMC and two potential sources of lipids in atheroma, i.e., lipoproteins and non-lipoprotein lipid droplets, could be governed by different components of the MP medium. In the

case of the lipid droplets, as modeled here in the form of **liposomes**, macrophage-derived lipoprotein **lipase** could play a major role in cholesteryl ester transfer into SMC.

L12 ANSWER 15 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:385218 BIOSIS
DOCUMENT NUMBER: PREV199396060518
TITLE: Apolipoprotein E modulates low density lipoprotein retention by lipoprotein **lipase** anchored to the subendothelial matrix.
AUTHOR(S): Saxena, Uday (1); Ferguson, Erika; Bisgaier, Charles L.
CORPORATE SOURCE: (1) Atherosclerosis Pharmacology, Parke-Davis Pharmaceutical Res., 2800 Plymmoth Road, Ann Arbor, MI 48105 USA
SOURCE: Journal of Biological Chemistry, (1993) Vol. 268, No. 20, pp. 14812-14819.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Lipoprotein **lipase** (**lipase**), a key enzyme in lipoprotein triglyceride metabolism, has been shown to markedly increase low density lipoprotein (LDL) retention by subendothelial matrix. In the present study we assessed the role that lipoprotein and matrix components play in retention of LDL by **lipase** anchored to the subendothelial matrix. **Lipase** addition to subendothelial matrix increased LDL retention by 66-fold. Scatchard analysis of LDL binding to **lipase**-containing matrix yielded an association constant of 12 nM. Exogenous addition of the matrix components, heparan sulfate and dermatan sulfate (i. e. chondroitin sulfate B), reduced LDL retention by greater than 90%. These glycosaminoglycans (GAGs) also reduced lipolytic activity associated with the matrix, suggesting that **lipase** was released from its binding sites on the matrix. In contrast, other matrix components (collagen, fibronectin, vitronectin, and chondroitin sulfate A) neither affected LDL release nor matrix lipolytic activity. Thus, heparan sulfate and dermatan sulfate function to anchor **lipase** to the subendothelial cell matrix. The effects of apolipoprotein E (apoE) and apoA-I were also examined. Preincubation of the subendothelial matrix with apoE, followed by washing, did not affect subsequent **lipase** binding to the matrix nor its ability to retain LDL. However, the direct addition of apoE alone or in combination with phospholipid **liposomes** decreased **lipase**-mediated LDL retention in a concentration-dependent fashion. Addition of apoA-I had no effect. Thus, in these studies apoE functions to displace LDL bound to **lipase**, but not **lipase** anchored to the matrix. To further examine the physiologic implications of this process, we assessed the ability of human apoE-rich and apoE-poor

high density lipoproteins (HDL) to displace LDL from matrix-anchored **lipase**. ApoE-rich HDL reduced LDL retention dramatically (86% at 2.5 mu-g/ml). In contrast, apoE-poor HDL, at the highest concentration evaluated (400 mu-g/ ml), decreased LDL retention by only 32%. Overall, these data suggest apoE and specifically apoE-containing HDL reduce the **lipase**-mediated retention of LDL by subendothelial matrix. This observation, in part could explain the protective effects of apoE and apoE-containing HDL against atherosclerosis.

L12 ANSWER 16 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:521995 BIOSIS
DOCUMENT NUMBER: PREV199396135402
TITLE: Purification and characterization of lipoprotein **lipase** from the white adipose, skeletal muscle, cardiac muscle, mammary gland and lung tissues of the rat.
AUTHOR(S): Soteriou, Antonhy; Cryer, Anthony (1)
CORPORATE SOURCE: (1) Dep. Biochem., Univ. Wales Coll. Cardiff, P.O. Box 903, Cardiff CF1 1ST UK
SOURCE: International Journal of Biochemistry, (1993) Vol. 25, No. 10, pp. 1483-1490.
ISSN: 0020-711X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB 1. Lipoprotein **lipase** (LPL) was isolated from five rat tissues: white adipose, skeletal muscle, cardiac muscle, mammary gland and lung. 2. Specific activity of the preparations varied from 75 U/mg for skeletal muscle and 720 U/mg for adipose. 3. The preparations were further analysed using SDS-PAGE and a single component identified. The mol. wt of 61,000 Da of this component was consistent for all five of the tissue sources. 4. Significant differences in the values of the isoelectric points of the enzyme species were revealed. The values varied from 7.23 (SEM 0.022) for cardiac and lung to 7.51 (SEM 0.037) for mammary. 5. Two-dimensional electrophoresis, using isoelectric focusing in the first dimension and SDS-PAGE in the second revealed differences in the patterns of stained material derived from the five tissue sources.

L12 ANSWER 17 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1994:66609 BIOSIS
DOCUMENT NUMBER: PREV199497079609
TITLE: Lipid absorption: Passing through the unstirred layers, brush-border membrane, and beyond.
AUTHOR(S): Thomson, A. B. R. (1); Schoeller, C.; Keelan, M.; Smith, L.; Clandinin, M. T.
CORPORATE SOURCE: (1) Nutr. Metab. Res. Group, Div. Gastroenterol., Dep. Med., 519 Robert Newton Res. Build., Univ. Alberta, Edmonton, AB T6G 2C2 Canada

SOURCE: Canadian Journal of Physiology and Pharmacology, (1993) Vol. 71, No. 8, pp. 531-555.
ISSN: 0008-4212.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Lipids are components of our diet and luminal secretions, with physicochemical characteristics that determine their digestion and absorption in the gastrointestinal tract. Lipids include triglycerides, phospholipids, and cholesterol. Dietary lipids contain approximately 97% triglycerides, with small amounts of phospholipids and cholesterol. These components are important in cell membrane composition, fluidity, peroxidation, prostaglandin and leukotriene synthesis, and cellular metabolic processes. Lipids are implicated in the mechanisms of brain development, inflammatory processes, atherosclerosis, carcinogenesis, aging, and cell renewal. Duodenal hydrolysis of dietary lipids and biliary phospholipids and cholesterol is carried out by pancreatic **lipase**, colipase, phospholipase A-2, and cholesterol esterase. Bile acid solubilization results in mixed micelles and **liposomes**, in gel and liquid crystal phases. Lipid digestion products pass across the intestinal unstirred water layer. For long-chain fatty acids and cholesterol, passage across the unstirred water layer is rate limiting, whereas passage of short- and medium-chain fatty acids is limited by the brush-border membrane. Within the unstirred water layer, an acidic microclimate aids micellar dissociation so that protonated, and to a lesser extent, nonprotonated monomers then pass across the intestinal brush-border membrane. Absorptive mechanisms have been studied extensively in relation to lipid composition, fatty acid chain length, degree of unsaturation, essential fatty acid content, phospholipid components, and cholesterol. Enterocytes may take up lipids from the intestinal lumen or from lipoproteins of the bloodstream, but these pools are likely to be functionally distinct. Recent advances are reviewed, including recent advances in the area of microclimates, compartmentation, lipid binding proteins, intracellular trafficking, intestinal lipoproteins, release of lipids across the basolateral membrane, and dietary effects.

L12 ANSWER 18 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1993:296149 BIOSIS
DOCUMENT NUMBER: PREV199396014374
TITLE: Uptake and transport of fluorescent derivatives of dolichol in human fibroblasts.
AUTHOR(S): Jiang, Liang W.; Mitchell, Barry A.; Teodoro, Jose G.; Rip, Jack W. (1)
CORPORATE SOURCE: (1) Children's Psychiatric Res. Inst., 600 Sanatorium Road, London, ON N6H 3W7 Canada
SOURCE: Biochimica et Biophysica Acta, (1993) Vol. 1147, No. 2, pp. 205-213.

ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English

AB We are using fluorescent derivatives to visualize the endocytic transport of dolichol intermediates from the cell surface to the lysosome, and to estimate their rate of turnover within the lysosome. Anthroyl dolichol and anthroyl (1-14C)dolichol were synthesized and purified by chromatography on silica and C-18 Sep-Paks followed by high-performance liquid chromatography on C-18. The successful synthesis of anthroyl polyisoprenoid alcohols was confirmed by the use of uv-visible spectrometry and by fluorescence spectrometry. The purified esters were taken up into Ham's media containing 10-30% fetal calf serum or alternatively reconstituted into phospholipid **liposomes** for delivery to human fibroblasts in culture. The uptake of fluorescent dolichol esters into the cell and into lysosomes was demonstrated using fluorescence microscopy. The localization of anthroyl dolichol in lysosomes was further documented by simultaneously labeling fibroblasts with anthroyl dolichol and FITC-dextran a recognized lysosomal marker. Fibroblasts generally showed several groupings (domains) of lysosomes, some were dually labeled while others were labeled exclusively with either anthroyl dolichol or FITC-dextran. Labeling with anthroyl dolichol was very slow relative to labeling of the same fibroblasts with FITC-dextran suggesting that anthroyl dolichol acts as a labeling agent for intracellular membranes, particularly those of the lysosome while the dextran fluorescence is presumably of lysosolic origin. Several types of experiments were done with anthroyl (1-14C)dolichol to establish that the fluorescence seen in lysosomes represents anthroyl dolichol. Anthroyl dolichol appears to enter fibroblasts intact, since we were unable to recover any free (1-14C)dolichol from total lipid extracts of (i) media used for the uptake of anthroyl dolichol or (ii) the media removed from cells labelled for 42 h. In addition, attempts to hydrolyze anthroyl (1-14C)dolichol in vitro using whole fibroblast homogenates at pH 4.0 and 7.5 were unsuccessful, even though the fibroblasts expressed acid **lipase** activity using 4-methylumbelliferyl palmitate as substrate.

L12 ANSWER 19 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:297600 BIOSIS
DOCUMENT NUMBER: PREV199396015825
TITLE: Chymotryptic cleavage of lipoprotein **lipase** : Identification of cleavage sites and functional studies of the truncated molecule.
AUTHOR(S): Lookene, Aviar; Bengtsson-Olivercrona, Gunilla (1)
CORPORATE SOURCE: (1) Dep. Med. Biochem. Biophysics, Univ. Umea, S-9801 87 Umea Sweden
SOURCE: European Journal of Biochemistry, (1993) Vol. 213, No. 1, pp. 185-194.
Searcher : Shears 308-4994

ISSN: 0014-2956.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Treatment of bovine lipoprotein **lipase** (LPL) with chymotrypsin results in cleavage between residues Phe390-Ser391 and between Trp392-Ser393, indicating that this region is exposed in the native conformation of LPL. Two main fragments are generated, one large including the amino-terminus (chymotrypsin-truncated LPL = c-LPL) and one small, carboxy-terminal fragment. The small fragment is not stable, but is further degraded by the protease. Isolated c-LPL has full catalytic activity against tributyryl glycerol (tributyrin) and p-nitrophenyl butyrate, while the activity against emulsions of long-chain triacylglycerols and against **liposomes** is reduced and the activity against milk fat globules and chylomicrons is lost. Several properties of c-LPL were investigated. It was found that c-LPL interacts with apolipoprotein CII (apo CII) as efficiently as intact LPL. The truncated enzyme bound to **liposomes** and to emulsions of long-chain triacylglycerols as well as the intact enzyme did. In contrast, c-LPL did not bind to milk fat globules or to chylomicrons. The activity of c-LPL was more sensitive to inhibition by other lipid-binding proteins, e.g. apolipoprotein CIII (apo CIII), than was the intact enzyme. The affinity for heparin was as high with c-LPL as with intact LPL. Like intact LPL, c-LPL is dimeric in its active form, as evidenced by sucrose density gradient centrifugation. It is concluded that the reduced catalytic and lipid-binding properties of c-LPL compared with intact LPL are related to the properties of the substrate interface. It is speculated that the carboxy-terminal part of LPL contains a secondary lipid-binding site, which is important for activity against chylomicrons and related substrates.

L12 ANSWER 20 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1993:2568 BIOSIS
DOCUMENT NUMBER: PREV199395002568
TITLE: Phosphatidylethanolamine:dolichol acyltransferase: Characterization and partial purification of a novel rat liver enzyme.
AUTHOR(S): Sindelar, Pavel; Chojnack, Tadeuz; Valtersson, Conny (1)
CORPORATE SOURCE: (1) Clinical Res. Centre, Huddinge Hosp., Karolinska Inst., S-141 86 Stockholm Sweden
SOURCE: Journal of Biological Chemistry, (1992) Vol. 267, No. 29, pp. 20594-20599.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Incubation of rat or human post-heparin plasma with (3H)dolichol incorporated in **liposomes** consisting of dioleoyl

phosphatidylcholine:dioleoyl phosphatidyl-ethanolamine (3:1) resulted in the formation of radioactive dolichyl oleate. Non-heparinized plasma did not esterify dolichol, and, hence, the enzyme involved is probably associated with the cell surface and released into the blood by heparin. The major location of this activity was the liver, and, therefore, a partial purification of the enzyme from heparinized rat liver perfusates was performed using DEAE-Sephacel and heparin-Sepharose chromatography. The dolichol acyltransferase activity copurified with hepatic **lipase** activity in a lipid-protein complex of 350 kDa. Optimal acylation is achieved at pH 7.5 in the presence of 5% plasma and 20 mM Ca-2+. Esterification can only be obtained when dolichol is present in a phospholipid bilayer, and the reaction is strongly stimulated by unsaturated phosphatidylethanolamine or phosphatidylserine. Radiolabeling experiments demonstrated that the primary acyl donor is phosphatidylethanolamine from which the fatty acid is transferred exclusively from position 1. Neither cholesterol nor retinol are esterified by the enzyme, and the reaction is not stimulated by acyl-CoA. Both the extracellular localization and the mechanism of transacylation clearly distinguish this new enzyme from the acyl-CoA:dolichol acyltransferase described earlier in microsomes.

L12 ANSWER 21 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1992:483706 BIOSIS
DOCUMENT NUMBER: BA94:115081
TITLE: TCDD 2 3 7 8 TETRACHLORODIBENZO-P-DIOXIN CAUSES REDUCTION IN GLUCOSE UPTAKE THROUGH GLUCOSE TRANSPORTERS ON THE PLASMA MEMBRANE OF THE GUINEA-PIG ADIPOCYTE.
AUTHOR(S): ENAN E; LIU P C C; MATSUMURA F
CORPORATE SOURCE: DEP. ENVIRONMENTAL TOXICOL., UNIV. OF CALIFORNIA, DAVIS, CALIF. 95620.
SOURCE: J ENVIRON SCI HEALTH PART B PESTIC FOOD CONTAM AGRIC WASTES, (1992) 27 (5), 495-510.
CODEN: JPFCD2. ISSN: 0360-1234.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB A single dose of 2,3,7,8-TCDD (1 .mu.g/kg, i.p. injection) resulted in a significant decrease in cellular 3-O-methyl-[3H]-glucose uptake by guinea pig adipose tissue and pancreas after 24 hours. An in situ tissue culture study in which pieces of adipose tissues were incubated with 10-8M TCDD showed a time-dependent decrease in glucose uptake. Reconstitution of adipocyte plasma membrane from tested or control animals into artificial **liposomes** also resulted in this difference in glucose uptake. Binding of [3H]-cytochalasin B, a specific inhibitor of glucose transporter proteins, was significantly lower in aectone-ether powder preparations of TCDD-treated adipose tissue than from controls, suggesting that the total titer of these proteins is decreased by

TCDD. Finally, the relevance of these results to glucose or lipid metabolism was tested. Lipoprotein **lipase** (LPL) activity of guinea pig adipose tissue was decreased after 8 hours in situ incubation with TCDD indicating that glucose uptake was depressed at an earlier time point. These findings may contribute to a better understanding of dioxin-induced "wasting syndrome".

L12 ANSWER 22 OF 33 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92369083 MEDLINE
DOCUMENT NUMBER: 92369083
TITLE: Amphotericin B-phospholipid interactions responsible for reduced **mammalian** cell toxicity.
AUTHOR: Perkins W R; Minchey S R; Boni L T; Swenson C E; Popescu M C; Pasternack R F; Janoff A S
CORPORATE SOURCE: Liposome Company, Inc., Princeton, NJ..
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1992 Jun 30) 1107 (2) 271-82.
Journal code: A0W. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199211
AB When interacting with phospholipid in an aqueous environment, amphotericin B forms unusual structures of markedly reduced toxicity (Janoff et al. (1988) Proc. Natl. Acad. Sci. USA 85, 6122-6126). These structures, which appear ribbon-like by freeze-fracture electron microscopy (EM), are found exclusively at amphotericin B to lipid mole ratios of 1:3 to 1:1. At lower mole ratios they occur in combination with **liposomes**. Circular dichroism (CD) spectra revealed two distinct modes of lipid-amphotericin B interaction, one for **liposomes** and one for the ribbon-like structures. In isolated **liposomes**, amphotericin B which comprised 3-4 mole percent of the bulk lipid was monomeric and exhibited a hemolytic activity comparable to amphotericin B suspended in deoxycholate. Above 3-4 mole percent amphotericin B, ribbon-like structures emerged and CD spectra indicated drug-lipid complexation. Minimal inhibitory concentrations for Candida albicans of **liposomal** and complexed amphotericin B were comparable and could be attributed to amphotericin a release as a result of lipid breakdown within the ribbon-like material by a heat labile extracellular yeast product (**lipase**). Negative stain EM of the ribbon-like structures indicated that the ribbon-like appearance seen by freeze-fracture EM arises as a consequence of the cross-fracturing of what are aggregated, collapsed single lamellar, presumably interdigitated, membranes. Studies examining complexation of amphotericin B with either DMPC or DMPG demonstrated that headgroup interactions played little role in the formation of the ribbon-like structures. With these results we propose that

ribbon-like structures result from phase separation of amphotericin B-phospholipid complexes within the phospholipid matrix such that amphotericin B release, and thus acute toxicity, is curtailed. Formation of amphotericin B-lipid structures such as those described here indicates a possible new role for lipid as a stabilizing matrix for drug delivery of lipophilic substances, specifically where a highly ordered packing arrangement between lipid and compound can be achieved.

L12 ANSWER 23 OF 33 MEDLINE
ACCESSION NUMBER: 91255233 MEDLINE
DOCUMENT NUMBER: 91255233
TITLE: Action of a microbial **lipase** /acyltransferase on phospholipid monolayers.
AUTHOR: Hilton S; Buckley J T
CORPORATE SOURCE: Department of Biochemistry and Microbiology, University of Victoria, British Columbia, Canada.
SOURCE: BIOCHEMISTRY, (1991 Jun 18) 30 (24) 6070-4. Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
AB Vibrio species release a **lipase** which shares many properties with **mammalian** lecithin-cholesterol acyltransferase. We have studied the action of the enzyme on phospholipid monolayers. At similar surface pressures, reaction velocities were higher with monolayers of dilauroylphosphatidylcholine than with the corresponding phosphatidylglycerol or phosphatidylethanolamine. The dependence of reaction velocity on molecular density was very similar for phosphatidylcholine and phosphatidylethanolamine monolayers. Lag times were shortest with phosphatidylglycerol at low molecular densities, but maximum velocity was reached at considerably lower densities than with the other two lipids. We have found [Hilton, S., McCubbin, N. D., Kay, C., & Buckley, J.T. (1990) Biochemistry 29, 9072-9078] that nicking of the enzyme with trypsin or other proteases results in an increase in its activity against lipids in membranes. Here we show that trypsin treatment results in a large change in the surface activity of the **lipase**, allowing it to penetrate monolayers at pressures higher than 40 mN.m-1.

L12 ANSWER 24 OF 33 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 91:136016 SCISEARCH
THE GENUINE ARTICLE: FA694
TITLE: **MAMMALIAN** ADIPOSE-TISSUE AND MUSCLE ARE MAJOR SOURCES OF LIPID TRANSFER PROTEIN MESSENGER-RNA

Searcher : Shears 308-4994

AUTHOR: JIANG X C; MOULIN P; QUINET E; GOLDBERG I J; YACOUB L K; AGELLON L B; COMPTON D; SCHNITZERPOLOKOFF R; TALL A R (Reprint)
CORPORATE SOURCE: COLUMBIA UNIV, DEPT MED, DIV MOLEC MED, NEW YORK, NY, 10032; SCHERING PLOUGH RES CORP, CARDIOVASC PHARMACOL, BLOOMFIELD, NJ, 07003; COLUMBIA UNIV, DEPT MED, DIV METAB, NEW YORK, NY, 10032
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991) Vol. 266, No. 7, pp. 4631-4639.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The plasma cholesteryl ester transfer protein (CETP) catalyzes the transfer of cholesteryl esters from high density lipoproteins (HDL) to triglyceride-rich lipoproteins and plays a major role in the catabolism of HDL. Lipoprotein **lipase** (LPL) is the rate-limiting enzyme for hydrolysis of circulating triglyceride and is involved in HDL formation. We show that tissues containing LPL are major sources of CETP mRNA in several **mammalian** species, including some with low cholesteryl ester transfer activity in plasma. In hamsters, adipose tissue and heart were found to be the richest sources of both CETP and LPL mRNA; in situ hybridization studies showed that the same cell types (i.e. adipocytes or myocytes) contained CETP and LPL mRNA in these tissues. Isolated adipocytes synthesized active CETP. Dietary studies revealed a complex pattern of response of CETP mRNA levels in different tissues, which showed partial similarity to the changes in LPL mRNA abundance. However, high cholesterol diets resulted in increased CETP mRNA abundance in adipose tissue, heart, and skeletal muscle, without equivalent changes in LPL mRNA. Plasma HDL cholesteryl ester levels showed strong inverse correlations with CETP mRNA abundance in adipose tissue.

The results suggest a conserved function of CETP in adipose tissue and heart, such as a co-ordinate action with LPL to enhance HDL turnover. Although there is considerable overlap in the tissue- and cell-specific pattern of CETP and LPL gene expression, dietary studies revealed only limited parallelism in response at the mRNA level. The increase in CETP mRNA in peripheral tissues in response to increased dietary cholesterol suggests that local induction of CETP synthesis may help to recycle cholesterol deposited in these tissues during lipolysis of dietary lipoproteins.

L12 ANSWER 25 OF 33 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 920098063 JICST-EPlus
TITLE: The role of free radicals and the effect of **liposomal** SOD in experimental pancreatitis.
Searcher : Shears 308-4994

AUTHOR: KENMOCHI TAKASHI; ASANO TAKEHIDE; ARITA SEIJI; NAKAGORI TOSHIO; ISONO KAICHI FUKUOKA TOSHIYUKI
CORPORATE SOURCE: Chiba Univ., School of Medicine Nara Medical Univ.
SOURCE: Suizo (Journal of the Japan Pancreas Society), (1991) vol. 6, no. 6, pp. 589-595. Journal Code: X0203A (Fig. 5, Ref. 19) ISSN: 0913-0071
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB The role of free radicals and the effect of **liposomal** SOD were studied in rat pancreatitis induced by closed duodenal loop. The experimental animals were divided into the following two groups: Group S **Liposomal** SOD at the dose of 2mg/100g was intramuscularly given to rats thirty minutes before the onset of pancreatitis; and Group C control group. Serum amylase and **lipase** levels three hours after the onset of pancreatitis in Group S were significantly lower than in Group C, and tissue blood flow rate 24hours after the onset of pancreatitis in Group S was significantly ligher than in Group C. In histological findings on the pancreas 24hours after the onset, severe bleeding was observed in Group C, while only slight bleeding was seen in Group S. The above suggests that free radicals should have a role in development of acute pancreatitis, and free radical scavenger (**liposomal** SOD) should be a potent treatment agent for acute pancreatitis. (author abst.)

L12 ANSWER 26 OF 33 CABA COPYRIGHT 2000 CABI
ACCESSION NUMBER: 91:105930 CABA
DOCUMENT NUMBER: 911436273
TITLE: Long-term prevention of atherosclerosis Prophylaxie a long terme de l'atherosclerose
AUTHOR: Hauton, J. C.
CORPORATE SOURCE: INSERM U-130, 10 avenue Viton, 13009 Marseille, France.
SOURCE: Cahiers de Nutrition et de Dietetique, (1990) Vol. 25, No. 2, pp. 87-91. 22 ref.
DOCUMENT TYPE: Journal
LANGUAGE: French
SUMMARY LANGUAGE: English
AB Research on human nutrition has shown a relation between food eaten and certain pathological states. This relation is well established between lipid intake and atherosclerosis. As an alternative to radical change in diet the introduction of a competitive interfacial phase into the intestine to trap **lipases** and bile salts is proposed. This would decrease the association between these

substances and the intraluminal triacylglycerol emulsion thus reducing the efficiency of lipolysis and reducing the formation of the intestinal micellar phase. The addition of a new type of **liposome** prepared with natural food to the diet could be a safe and efficient way of preventing atherosclerosis without using drugs.

L12 ANSWER 27 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1980:286096 BIOSIS
DOCUMENT NUMBER: BA70:78592
TITLE: THE MURINE MACROPHAGE FC RECEPTOR FOR IMMUNO GLOBULIN G-2B IS LIPID DEPENDENT.
AUTHOR(S): ANDERSON C L
CORPORATE SOURCE: DEP. MED., UNIV. ROCHESTER, ROCHESTER, N.Y. 14642, USA.
SOURCE: J IMMUNOL, (1980) 125 (2), 538-540.
CODEN: JOIMA3. ISSN: 0022-1767.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The plasma membrane Fc receptor for **Ig**[**immunoglobulin**]G2b on [murine macrophage-like] P388D1 cells, solubilized by detergent, was inactivated by incubation with phospholipase C. Soluble Fc receptor activity could be restored by the addition of **liposomes** of phosphatidylethanolamine or phosphatidylinositol. The reconstituted Fc receptor was trypsin sensitive. Fc receptor binding of IgG2b apparently from the concerted action of membrane lipid and protein.

L12 ANSWER 28 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1981:168656 BIOSIS
DOCUMENT NUMBER: BA71:38648
TITLE: LAMELLAR GRANULES IN **MAMMALIAN** **AVIAN** AND REPTILIAN EPIDERMIS.
AUTHOR(S): LANDMANN L
CORPORATE SOURCE: DEP. OF ANATOMY, UNIV. OF BASEL, PESTALOZZISTR. 20, CH-4056 BASEL, SWITZERLAND.
SOURCE: J ULTRASTRUCT RES, (1980) 72 (3), 245-263.
CODEN: JULRA7. ISSN: 0022-5320.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Evidence is presented that **mammalian** membrane-coating granules [from neonatal mice] **avian** multigranular bodies [from chicken] and reptilian mesos granules [from grass snake, Natrix natrix] are homologous structures. All 3 types, which will here be called lamellar granules, have the following items in common: a lamellar pattern produced by disks stacked coin-like above each other, major dense lines separating adjacent disks, each of which contains a minor dense line, spacing between and thickness of major dense lines, positive reaction with various lipid stains,

periodic acid-Schiff and the Thiery Ag method, disappearance of the lamellar pattern after treatment with lipid solvents or phospholipase C, and extrusion of contents into the intercellular space and its rearrangement into broad sheets running parallel to the surface of the horny cells. Based on these obseervations and previous biochemical results, the lamellar contents (disks) are interpreted as flattened **liposomes**.

L12 ANSWER 29 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1980:267640 BIOSIS
DOCUMENT NUMBER: BA70:60136
TITLE: STEPWISE DEGRADATION OF MEMBRANE SPHINGOMYELIN BY CORYNEBACTERIAL PHOSPHO **LIPASES**.
AUTHOR(S): BERNHEIMER A W; LINDER R; AVIGAD L S
CORPORATE SOURCE: DEP. MICROBIOL., N.Y. UNIV. SCH. MED., NEW YORK, N.Y. 10016, USA.
SOURCE: INFECT IMMUN, (1980) 29 (1), 123-131.
CODEN: INFIBR. ISSN: 0019-9567.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The mechanism of in vitro synergistic lysis of sheep erythrocytes by Corynebacterium ovis [C. pseudotuberculosis] and C. equi was investigated. Hemolysis required the action of phospholipase D from C. ovis, the action of an extracellular protein of C. equi and Mg2+. Maximum lysis required imposition on the system of a 4th condition such as chilling. The extracellular protein of C. equi was purified to homogeneity and was a phospholipase C capable of hydrolyzing ceramide phosphate, phosphatidic acid and all of the isolated major phospholipids of **mammalian** erythrocyte membranes. The principal features of the synergistic hemolytic system could be reproduced in experiments involving **liposomes** containing sphingomyelin or ceramide phosphate and trapped [14C]glucose. Sphingomyelin of sheep erythrocytes may be first converted to ceramide phosphate by C. ovis phospholipase D. The ceramide phosphate may be converted to ceramide by C. equi phospholipase C. The resulting in situ ceramide then may undergo dislocation by chilling and perhaps by virtue of an affinity between ceramide and C. equi phospholipase C. The dislocation of ceramide presumably disorganizes the lipid bilayer sufficiently to result in cell lysis.

L12 ANSWER 30 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1980:175962 BIOSIS
DOCUMENT NUMBER: BA69:50958
TITLE: CYTO TOXICITY OF HUMAN MONONUCLEAR CELLS AGAINST CHICKEN AND HUMAN RED BLOOD CELLS INDUCED BY TREATMENT OF THE EFFECTOR CELLS WITH PHOSPHO **LIPASE** C.
AUTHOR(S): NORTHOFF H; RESCH K
CORPORATE SOURCE: INST. IMMUNOL. SEROL., IM NEUENHEIMER FELD 305,

D-6900 HEIDELBERG, W. GER.
SOURCE: EUR J IMMUNOL, (1979) 9 (10), 757-761.
CODEN: EJIMAF. ISSN: 0014-2980.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Human mononuclear cells from peripheral blood which were treated with phospholipase C (PLC), became cytotoxic against human or chicken red blood cells [RBC]. PLC-induced cellular cytotoxicity against human RBC was further analyzed and compared to anti-D-mediated, antibody-dependent cellular cytotoxicity (ADCC), using the same target cells. ADCC, but not cytotoxicity of PLC-treated effector cells, was inhibited by free **Ig**[**immunoglobulin**]G. Iodoacetate strongly enhanced PLC-induced cytotoxicity, but blocked ADCC completely. Addition of fetal calf serum or human AB serum impaired PLC-induced cytotoxicity. A similar inhibition was found by adding lecithin **liposomes** suggesting that the inhibitory effect of sera was also due to their phospholipid content. Cytotoxicity of PLC-treated effector cells could be clearly distinguished from cellular cytotoxicity, occurring spontaneously or induced by target cell antibodies. Cytotoxicity of PLC-treated effector cells against human erythrocytes is apparently due to the action of PLC, adsorbed to the effector cells.

L12 ANSWER 31 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1979:268132 BIOSIS
DOCUMENT NUMBER: BA68:70636
TITLE: A CYTOLYTIC PROTEIN FROM THE EDIBLE MUSHROOM PLEUROTUS-OSTREATUS.
AUTHOR(S): BERNHEIMER A W; AVIGAD L S
CORPORATE SOURCE: DEP. MICROBIOL., N.Y. UNIV. SCH. MED., NEW YORK, N.Y. 10016, USA.
SOURCE: BIOCHIM BIOPHYS ACTA, (1979) 585 (3), 451-461.
CODEN: BBACAQ. ISSN: 0006-3002.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Aqueous extracts of the edible mushroom, Pleurotus ostreatus, contain a substance that is lytic in vitro for **mammalian** erythrocytes. The hemolytic agent, pleurotolysin, was purified to homogeneity and is a protein lacking 7 of the amino acids commonly found in proteins. In the presence of sodium dodecyl sulfate it exists as monomers of MW 12,050; under non-dissociating conditions it exists as dimers. It is isoelectric at about pH 6.4. The sensitivity of erythrocytes from different animals correlates with sphingomyelin content of the erythrocyte membranes. Sheep erythrocyte membranes inhibit pleurotolysin-induced hemolysis and the inhibition is time and temperature dependent. Ability of membranes to inhibit hemolysis is abolished by prior treatment of membranes with specific phospholipases. Pleurotolysin-induced hemolysis is inhibited by **liposomes** prepared from

cholesterol, dicetyl phosphate and sphingomyelin derived from sheep erythrocytes whereas a variety of other lipid preparations fail to inhibit. Sphingomyelin plays a key role in the hemolytic reaction.

L12 ANSWER 32 OF 33 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1980:166613 BIOSIS
DOCUMENT NUMBER: BA69:41609
TITLE: THE INVOLVEMENT OF THE LIPID PHASE TRANSITION IN THE PLASMA INDUCED DISSOLUTION OF MULTI LAMELLAR PHOSPHATIDYL CHOLINE VESICLES.
AUTHOR(S): SCHERPHOF G; MORSELT H; REGTS J; WILSCHUT J C
CORPORATE SOURCE: LAB. PHYSIOL. CHEM., UNIV. GRONINGEN, BLOEMSINGEL 10, 9712 KZ GRONINGEN, NETH.
SOURCE: BIOCHIM BIOPHYS ACTA, (1979) 556 (2), 196-207.
CODEN: BBACAQ. ISSN: 0006-3002.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Unsonicated **liposomes** prepared from dimyristoyl phosphatidylcholine were nearly completely dissolved during a 3 h incubation with rat plasma at or close to the phase-transition temperature of 24.degree. C. At 37.degree. or 15.degree. C virtually no **liposomal** disintegration was observed even after 24 h of incubation. The **liposomal** solubilization, which was monitored by turbidity measurements or by determination of phospholipid sedimentability, was accompanied by the formation of a phospholipid-protein complex similar or identical to the one previously reported to be formed from sonicated **liposomes** of egg phosphatidylcholine. Unsonicated multilamellar **liposomes** made of egg phosphatidylcholine were completely resistant to the dissolving potency of plasma when incubated at 37.degree. C. **Liposomes** from equimolar mixtures of dimyristoyl and dipalmitoyl phosphatidylcholine were only degraded by plasma in the temperature range between 30-35.degree. C at which temperature this cocrystallizing phospholipid mixture undergoes a phase transition. Even at these temperatures the rate of dissolution of this mixture was significantly lower than of dimyristoyl phosphatidylcholine at 24.degree. C. In the dissolving process of this mixture a slight preference for the lower-melting component was observed. The ability of cholesterol to completely abolish the susceptibility of dimyristoyl phosphatidylcholine **liposomes** to plasma at a 1 : 2 molar ratio of cholesterol to phospholipid substantitates the essential role of the phase transition in the process of **liposome** solubilization. When **liposomes** of the monotectic mixtures dimyristoyl and distearoyl phosphatidylcholine or dilauroyl and distearoyl phosphatidylcholine were incubated with plasma at temperatures in between those at which the constituent lipids undergo a phase change in the mixture, the **liposomes** were slowly dissolved. Under those conditions a selective removal of the lipids in the liquid-crystalline phase was

observed. For the plasma-induced dissolution of unsonicated **liposomes**, which is most probably achieved by interaction with (apo)lipoproteins, the presence of phase boundaries is required in much the same way as was first reported for phospholipases.

L12 ANSWER 33 OF 33 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-072228 [06] WPIDS
DOC. NO. CPI: C2000-020588
TITLE: Novel peptides for treating autoimmune diseases of central nervous system characterized by demyelination.
DERWENT CLASS: B04 D16
INVENTOR(S): ARIMILLI, S; DESHPANDE, S
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9957241	A2	19991111	(200006)*	EN	57

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9957241	A2	WO 1999-US9930	19990505

PRIORITY APPLN. INFO: US 1998-73109 19980505
AN 2000-072228 [06] WPIDS
AB WO 9957241 A UPAB: 20000203
NOVELTY - An isolated peptide derived from human myelin basic protein (MBP), is new.
DETAILED DESCRIPTION - Novel MBP peptides have an amino acid (aa) sequence (S1):
Phe-X-Lys-Asn-Ile-Val-X-X-X-Thr-X-X (S1)
X = any aa.
INDEPENDENT CLAIMS are also included for the following:
(1) an isolated nucleic acid (I), encoding (1);
(2) a composition (II), comprising a major histocompatibility complex (MHC) class II complex (IIa) capable of binding a T-cell receptor (TCR), and (IIa) consisting of:
(a) a MHC class II polypeptide comprising an extracellular

domain of a MHC class II molecule with an antigen (Ag) binding pocket, which is encoded by an allele associated with an autoimmune disease directed to MBP; and the class II component is soluble under physiological conditions in the absence of detergent or liquid;

(b) a MBP peptide having an aa sequence (S2); and

(c) the MBP peptide is bound to MHC class II component Ag binding pocket;

(3) an antibody (Ab) specifically immunoreactive under immunologically active conditions to a MBP peptide having an amino acid sequence (S3);

(4) a composition comprising (II); and

(5) identifying a T-cell epitope on an Ag which when bound to the Ag binding pocket of a MHC class II molecule, is capable of binding to a TCR and such binding triggers an extracellular acidification reaction by a T-cell expressing the TCR, by:

(a) providing a composition comprising the T-cell epitope bound to the Ag binding pocket of a MHC class II molecule;

(b) contacting a T-cell expressing the TCR, with the epitope; and

(c) measuring the extracellular acidification, in which a change in the extracellular acidification indicates the binding of T- cell epitope to the TCR.

Phe-X-Lys-R1-Ile-Val-X-X- X-Thr-X-X (S2)

R1 = Asn or Gln.

Phe-Phe-Lys-Asn-Ile-Val-Thr-Pro-Arg-Thr- Pro-Pro (S2)

ACTIVITY - Neuroprotective. No supporting data given.

MECHANISM OF ACTION - T-cell clonal anergy/tolerance inducer; Cytokine-mediated immunosuppressive immune response inducer.

USE - The MBP peptides are used in the treatment of autoimmune mediated demyelinating disease especially multiple sclerosis or the murine demyelinating experimental autoimmune encephalomyelitis. The therapeutic compositions comprising novel MBP peptides are used for inducing oral tolerance or general tolerance. The compositions are used to downregulate or eliminate autoreactive components of the immune system and treat autoreactive demyelinating, T-cell mediated immune response. The novel MBP peptides when administered into a subject are useful for inhibiting a T-cell mediated immune response against MBP, to treat the T-cell mediated immune response which causes a pathological condition of the nervous system e.g., multiple sclerosis (claimed).

ADVANTAGE - Prevention or suppression of MHC-restricted immune responses is done without any undesirable side effects, such as nonspecific suppression of an individual's overall immune response. The MBP peptides provide a safer and more effective treatment by selectively suppressing autoimmune responses at the helper CD4+ T-cell levels.

Dwg.0/8

FILE 'CAPLUS' ENTERED AT 12:03:06 ON 10 FEB 2000

Searcher : Shears 308-4994

L13 10 S L8 AND ANTIBOD?
L14 8 S L13 NOT L10

L14 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:779110 CAPLUS
DOCUMENT NUMBER: 132:40506
TITLE: Antiviral supramolecules containing target-binding molecules and therapeutic molecules bound to spectrin
INVENTOR(S): Virtanen, Jorma; Virtanen, Sinikka
PATENT ASSIGNEE(S): Burstein Laboratories, Inc., USA
SOURCE: U.S., 46 pp., Cont.-in-part of U.S. 5,718,915.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5997861	A	19991207	US 1996-627695	19960329
US 5718915	A	19980217	US 1995-424874	19950419
CA 2218691	AA	19961024	CA 1996-2218691	19960418
PRIORITY APPLN. INFO.:			US 1994-332514	19941031
			US 1995-424874	19950419
			US 1996-627695	19960101

AB Complexes are prepd. contg. two or more different effector mols. joined to each other by a joining component. One effector mol. is a binding mol. such as an **antibody** or Fc receptor that binds to a mol. target such as a virus or **antibody** at a site of infection or tumor, and another effector mol. is a therapeutic mol. such as an enzyme or drug. The joining component may be a **liposome**, protein or an org. polymer (including a dendrimer type polymer), and may be of sufficient length and/or flexibility to permit the therapeutic mol. to phys. interact with the target at the same time as the binding mol. Supramols. are formed contg. at least two supramol. component mols. that contain an effector mol. and a nucleic acid chain. A nucleic acid chain on a component mol. is complementary to a nucleic acid chain on another component mol. to enable binding of the component mols. of the supramol. by the formation of double stranded nucleic acid chains between complementary chains. A targetable antiviral supramol. is prepd. contg. spectrin as the joining component. The binding mol. can be an **antibody** specific for an antigen on a viral particle and the therapeutic mol. can be an enzyme capable of destroying infectivity of the virus by hydrolysis of viral coat protein or viral lipid.

IT **9001-62-1, Lipase**
RL: PEP (Physical, engineering or chemical process); THU

(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiviral supramols. contg. target-binding mols. and therapeutic mols. bound to spectrin)

L14 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:388630 CAPLUS
DOCUMENT NUMBER: 129:37207
TITLE: Transfecting composition usable in gene therapy containing viral vector and transfecting agent such as cationic polymers or lipofectants
INVENTOR(S): Aubailly, Nathalie; Benoit, Patrick; Branellec, Didier; Le Roux, Aude; Mahfoudi, Abderrahim; Ratet, Nathalie
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.; Aubailly, Nathalie; Benoit, Patrick; Branellec, Didier; Le Roux, Aude; Mahfoudi, Abderrahim; Ratet, Nathalie
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823765	A1	19980604	WO 1997-FR2157	19971128
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2756491	A1	19980605	FR 1996-14693	19961129
FR 2756491	B1	19990108		
AU 9874010	A1	19980622	AU 1998-74010	19971128
EP 948636	A1	19991013	EP 1997-948959	19971128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
NO 9902577	A	19990728	NO 1999-2577	19990528
PRIORITY APPLN. INFO.:			FR 1996-14693	19961129
			WO 1997-FR2157	19971128

AB The invention concerns a transfecting compn. usable in gene therapy characterized in that it combines one or several non-coated recombinant viruses and comprising in their genome at least an exogenous nucleic acid and at least one non-viral and non-plasmid transfecting agent. Use of lipofectants to improve transfection

efficiency and minimize immune reaction to adenoviral vector transfection of vascular smooth muscle cells was demonstrated.

IT **9001-62-1, Lipase**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(viral vector contg. gene for; transfecting compn. usable in gene therapy contg. viral vector and transfecting agent such as cationic polymers or lipofectants)

L14 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:650227 CAPLUS
DOCUMENT NUMBER: 127:304097
TITLE: Methods for increasing or decreasing the efficiency of transformation by controlling glycosaminoglycan and proteoglycan levels
INVENTOR(S): Mislick, Kimberly Ann
PATENT ASSIGNEE(S): California Institute of Technology, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734483	A1	19970925	WO 1997-US4217	19970312
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5783566	A	19980721	US 1996-644095	19960510
AU 9722145	A1	19971010	AU 1997-22145	19970312
PRIORITY APPLN. INFO.:			US 1996-13647	19960318
			US 1996-644095	19960510
			WO 1997-US4217	19970312

AB Methods for controlling the efficiency of transformation of animal cells with nucleic acid complexes with cationic substance by adjusting conçns. of membrane-assocd. proteoglycans and optionally adjusting the plasma concn. of glycosaminoglycans are described. By increasing the level of membrane-assocd. proteoglycans, e.g. with phorbol esters, growth factors, or cytokines, in the cell, and optionally decreasing the plasma concn. of glycosaminoglycans, e.g. with plasma lipoproteins or protease inhibitors, the transformation efficiency can be increased. By decreasing the level of

membrane-assocd. proteoglycans in the cell, and optionally decreasing the plasma concn. of glycosaminoglycans, the transformation efficiency can be decreased. Glycosaminoglycan biosynthesis inhibitors such as 2-deoxy-D-glucose can be used. Transfection efficiency can be controlled in vivo, ex vivo, or in vitro.

IT **9001-62-1, Lipase**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(lowering of plasma glycosaminoglycan levels using; methods for increasing or decreasing efficiency of transformation by controlling glycosaminoglycan and proteoglycan levels)

L14 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:748430 CAPLUS
DOCUMENT NUMBER: 126:14778
TITLE: Binding molecule complexes with two or more effector molecules, and therapeutic and other uses thereof
INVENTOR(S): Virtanen, Jorma; Virtanen, Sinikka
PATENT ASSIGNEE(S): Burstein Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9632841	A1	19961024	WO 1996-US5389	19960418
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5718915	A	19980217	US 1995-424874	19950419
AU 9655554	A1	19961107	AU 1996-55554	19960418
PRIORITY APPLN. INFO.:			US 1995-424874	19950419
			US 1994-332514	19941031
			WO 1996-US5389	19960418

AB Structures that bind to a selected target are prepd. having two or more different effector mols. joined to each other by a joining component. At least one of the effector mols. (e.g. an **antibody**) binds to the target and at least one of the other effector mols. (e.g. an enzyme) is therapeutic. The joining component may be a **liposome**, protein, dendrimer polymer or

complementary nucleic acid chains. The joining component may be of sufficient length and/or flexibility to permit the therapeutic mol. to phys. interact with the target at the same time as the binding mol. binds with the target. The structures may be used in disease treatment, immunoassays and sensors. For in vivo genetic manipulation of cells, the **liposome** joining component is filled with a plurality of genetic manipulation complexes that contain a polynucleotide having a sequence for recombination and a binding site, a DNA binding protein bound to the binding site and a motor protein conjugated to the polynucleotide. Prophospholipase may be on the surface of the **liposome**, and when activated cleaves the **liposome** to release the complex.

IT **9001-62-1**, **Lipase 9001-62-1D**,
Lipase, conjugates with maleimide polyethylene glycol
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding mol. complexes with two or more effector mols., and therapeutic and other uses thereof)

L14 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:646426 CAPLUS
DOCUMENT NUMBER: 125:284924
TITLE: Pharmaceuticals and assays using enzyme subunits
INVENTOR(S): Titball, Richard William; Carr, Francis Joseph
PATENT ASSIGNEE(S): Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9625952	A1	19960829	WO 1996-GB380	19960221
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2213566	AA	19960829	CA 1996-2213566	19960221
AU 9647259	A1	19960911	AU 1996-47259	19960221
EP 810880	A1	19971210	EP 1996-903111	19960221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
CN 1182372	A	19980520	CN 1996-193434	19960221
JP 11500136	T2	19990106	JP 1996-525485	19960221
ZA 9601427	A	19960807	ZA 1996-1427	19960222

PRIORITY APPLN. INFO.: GB 1995-3486 19950222
WO 1996-GB380 19960221

AB A method of releasing an agent (e.g. a chemotherapeutic) under predetd. conditions comprising the steps of protecting the agent within a lipid structure (e.g. a **liposome**), causing **lipase** activity to be constituted by combining two or more components (e.g. recombinant N- or C-terminal Clostridium perfringens alpha-toxin fragments), one of these components being conjugated to a targeting mol. (e.g. an **antibody**) which binds to a target (e.g. a tumor antigen) under the predetd. conditions. The lipid structure is then exposed to the constituted **lipase** activity such as to release the agent. Also disclosed are materials and kits for use in the method.

IT **9001-62-1, Lipase**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug-releasing formulations)

L14 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:432302 CAPLUS
DOCUMENT NUMBER: 121:32302
TITLE: Murine macrophages secrete factors that enhance uptake of non-lipoprotein [3H]cholesteryl ester by aortic smooth muscle cells
AUTHOR(S): Stein, O.; Ben-Naim, M.; Dabach, Y.; Hollander, G.; Stein, Y.
CORPORATE SOURCE: Department of Experimental Medicine and Cancer Research, Hebrew University-Hadassah Medical School, Jerusalem, Israel
SOURCE: Biochim. Biophys. Acta (1994), 1212(3), 305-10
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have recently demonstrated that macrophage conditioned medium (MP medium) and .beta.VLDL enhance cholesterol esterification in cultured aortic smooth muscle cells by LDL receptor mediated and other pathways. In view of the presence of extracellular non-lipoprotein cholesteryl ester (in the form of lipid droplets) in the atheroma, the effect of MP medium on the cellular uptake of **liposomal** cholesteryl linoleyl ether (CLE) or cholesteryl ester (CE) was studied. After 4 h incubation in MP medium, the uptake of **liposomal** [3H]CLE was up to 10-fold higher than in the presence of control medium of the same compn. but not conditioned with macrophages (DV medium). Similar results were seen also with HSF derived from LDL receptor neg. donors. The MP medium-stimulated uptake of **liposomal** [3H]CE resulted also in hydrolysis of 70-90% of the labeled compd., indicating that the [3H]CE was intracellular. While the MP medium effect on **liposomal** [3H]CLE uptake was evident after 4 h, its effect on [3H]cholesterol esterification by SMC in the presence of

.beta.VLDL could be demonstrated only after 24 h. Addn. of apoE to MP medium resulted in a small (30-40%) increase in the uptake of **liposomal** [3H]CLE; however, it was augmented more than 4-fold when apoE was added to DV medium. The MP medium effect on the uptake of **liposomal** [3H]CLE was interfered with by heparin, anti-LPL **antibody** or heparinase, while these treatments did not affect [3H]cholesterol esterification in the presence of .beta.VLDL. These results suggest that the interaction between SMC and two potential sources of lipids in atheroma, i.e., lipoproteins and non-lipoprotein lipid droplets, could be governed by different components of the MP medium. In the case of the lipid droplets, as modeled here in the form of **liposomes**, macrophage-derived lipoprotein **lipase** could play a major role in cholesteryl ester transfer into SMC.

L14 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1984:2629 CAPLUS
DOCUMENT NUMBER: 100:2629
TITLE: Lipoprotein **lipase**:apolipoprotein C-II interactions studied by fluorescence and monoclonal **antibodies**
AUTHOR(S): Smith, L. C.; Voyta, J. C.; Rohde, M. F.; Kinnunen, P. K. J.; Gotto, A. M., Jr.; Sparrow, J. T.
CORPORATE SOURCE: Dep. Med., Methodist Hosp., Houston, TX, 77030, USA
SOURCE: Atherosclerosis (Berlin) (1983), 6, 636-9
CODEN: THRSDS; ISSN: 0170-0626
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The direct interaction of milk lipoprotein **lipase** (I) with apolipoprotein C-II (apoC-II) was investigated. Dansylated derivs. of apoC-II peptide fragments were prepd.; the assocn. of these peptides with I in the absence and presence of nonhydrolyzable lipid ether-contg. **liposomes** was detd. The Ka values increased >50-fold with increasing peptide chain length in the presence of the **liposomes**. In the absence of the **liposomes**, there was no chain length dependence after a 10-fold increase in Ka when the 15-residue dansylated peptide was lengthened by 4 residues. Three of 4 monoclonal **antibodies** against I inhibited the interaction of I with the dansylated peptide representing apoC-II residues 60-78. These **antibodies** recognized a 17,000-dalton CNBr fragment of I, thus suggesting that the apoC-II recognition site is located within this region of I.

L14 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:487714 CAPLUS
DOCUMENT NUMBER: 97:87714
TITLE: Immunological studies on bovine milk lipoprotein

lipase. Effects of Fab fragments on enzyme activity

AUTHOR(S): Shirai, Kohji; Wisner, Daniel A.; Johnson, J. David; Srivastava, Laxmi S.; Jackson, Richard L.

CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, 45267, USA

SOURCE: Biochim. Biophys. Acta (1982), 712(1), 10-20
CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rabbit antiserum against purified bovine milk lipoprotein **lipase** (I) was prepd. Immunoelectrophoresis of I gave a single precipitin line against the **antibody**; the line was coincident with enzyme activity. The .gamma.-globulin fraction inhibited heparin-releasable I activity of bovine arterial intima, heart, muscle, and adipose tissue. The **antibody** also inhibited the I activities of adipose tissue of human and pig, but not those of rat and dog. Fab fragments were prepd. by papain digestion of the .gamma.-globulin fraction. Fab fragments inhibited the I-catalyzed hydrolysis of dimyristoylphosphatidylcholine vesicles and triolein emulsions to the same extent. The Fab fragments also inhibited the lipolysis of human plasma very-low-d. lipoproteins. The change in the kinetic parameters for the I-catalyzed hydrolysis of triolein by the Fab fragments was accompanied by a 3-fold increase in Km and a 10-fold decrease in Vmax. Preincubation of I with apolipoprotein C-II, the activator protein for I, did not prevent inhibition of enzyme activity by the Fab fragments. However, preincubation with dipalmitoylphosphatidylcholine-emulsified triolein or Triton X-100-emulsified triolein had a protective effect (remaining activity 7.0 or 25.8%, resp., compared with 1.0 or 0.4% with no preincubation). The addn. of both apolipoprotein G-II and substrate prior to the incubation with the Fab fragments was assocd. with an increased protective effect against inhibition of enzyme activity; remaining activity with dipalmitoylphosphatidylcholine-emulsified triolein was 40.6% and with Triton X-100-emulsified triolein, 45.4%. Human plasma very-low-d. lipoproteins also protected against the inhibition of I activity by the Fab fragments. Apparently, the interaction of I with apolipoprotein C-II in the presence of lipids is assocd. with a conformational change in the structure of the enzyme such that the Fab fragments are less inhibitory. The consequence of a conformational change in I may be to facilitate the formation of an enzyme-triacylglycerol complex so as to enhance the rate of the I-catalyzed turnover of substrate to products.

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, CABA, AGRICOLA, FSTA' ENTERED AT 12:04:08 ON 10 FEB 2000)

L15 16 S L13

Searcher : Shears 308-4994

L16 12 S L15 NOT L11
L17 10 DUP REM L16 (2 DUPLICATES REMOVED)

L17 ANSWER 1 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-263358 [22] WPIDS
DOC. NO. NON-CPI: N1999-196174
DOC. NO. CPI: C1999-077579
TITLE: A new method to screen for potential drugs.
DERWENT CLASS: A96 B04 D16 S03
INVENTOR(S): SHORT, J M
PATENT ASSIGNEE(S): (DIVE-N) DIVERSA CORP
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9910539	A1	19990304	(199922)*	EN	54
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9889231	A	19990316	(199930)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9910539	A1	WO 1998-US17779	19980826
AU 9889231	A	AU 1998-89231	19980826

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9889231	A	Based on	WO 9910539

PRIORITY APPLN. INFO: US 1997-918406 19970826
AN 1999-263358 [22] WPIDS
AB WO 9910539 A UPAB: 19990609
NOVELTY - Identifying a desired activity encoded by a nucleic acid by screening expression libraries of uncultivated organisms, is new
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) identifying a desired activity encoded by a genomic DNA population, comprising:
(a) obtaining a single-stranded genomic DNA population;
(b) contacting the population with a DNA probe bound to a ligand under hybridisation conditions to obtain a double-stranded complex of probe:genomic DNA;
(c) contacting the obtained complex with a solid phase specific binding partner for the ligand to produce a solid phase complex;
(d) separating the solid phase complex from the single strand

population;

(e) releasing from the probe the members of the genomic population that bound to the solid phase bound probe;

(f) forming double-stranded DNA from the above genomic members;

(g) introducing the above double-stranded DNA into a suitable host cell to produce an expression library containing a plurality of clones containing the selected DNA;

(h) screening the expression library for the desired activity

(2) preselecting a desired DNA from a genomic DNA population, comprising:

(a) obtaining a single-stranded genomic DNA population;

(b) contacting the population with a ligand-bound oligonucleotide probe complementary to a secretion signal sequence unique to a given class of proteins under hybridisation conditions to form a double-stranded complex;

(c) contacting the obtained complex with a solid phase specific binding partner for the ligand to produce a solid phase complex;

(d) separating the solid phase complex from the single strand population;

(e) releasing from the probe the members of the genomic population that bound to the solid phase bound probe;

(f) forming double-stranded DNA from the above genomic members;

(g) introducing the above double-stranded DNA into a suitable host cell to produce an expression library containing a plurality of clones containing the selected DNA;

(h) screening the expression library for the desired activity;

(3) identifying a desired activity encoded by a nucleic acid population, comprising:

(a) generating one or more gene libraries derived from the population;

(b) combining extracts of the gene library(s) with target cell components obtained from metabolically rich cells, and

(c) screening the combination to identify the desired activity.

USE - The invention is used to screen for new bioactive compounds with potential for use as drugs such as antibiotics, anti-virals, anti-tumour agents and regulatory proteins.

ADVANTAGE - Unlike prior art, the invention allows one to clone using well known genetic systems, and to screen in vitro with crude preparations.

Dwg.0/9

L17 ANSWER 2 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER: 1998-169316 [15] WPIDS

DOC. NO. NON-CPI: N1998-134366

DOC. NO. CPI: C1998-054340

TITLE: Amplification or generation of detectable signal - by releasing signalling agent from vesicle as a result of reaction between probe and analyte, especially for hybridisation and immunoassays.

Searcher : Shears 308-4994

DERWENT CLASS: B04 D16 S03
INVENTOR(S): CARR, F
PATENT ASSIGNEE(S): (ECLA-N) ECLAGEN LTD; (BIOV-N) BIOVATION LTD
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9808097	A1	19980226	(199815)*	EN	32
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9740238	A	19980306	(199830)		
EP 922224	A1	19990616	(199928)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9808097	A1	WO 1997-GB2254	19970822
AU 9740238	A	AU 1997-40238	19970822
EP 922224	A1	EP 1997-937697	19970822
		WO 1997-GB2254	19970822

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9740238	A	Based on	WO 9808097
EP 922224	A1	Based on	WO 9808097

PRIORITY APPLN. INFO: GB 1996-17631 19960822
AN 1998-169316 [15] WPIDS
AB WO 9808097 A UPAB: 19980410
Amplification and/or generation of a signal for detecting a probe (I) comprises reacting (I) and test compound (II) and detecting reaction from release of a signalling agent (III) from within a vesicle. Also new are kits for detecting (I) comprising a vesicle containing (III).

(III) is in active, but ineffective form, and/or is deposited on a solid phase (particularly by reaction with a receptor) close to (I). (I) is directly or indirectly linked to a system that releases (III) from the vesicle, which is a **liposome**, any eukaryotic or prokaryotic cells (e.g. a red blood cell), lipid-based emulsion and/or artificial membrane. The system for release of (III)

is a **lipase**, galactosidase, detergent, animal complement and/or cytolysin, optionally as two subunits, one attached to (I) and the other to e.g. the vesicle. (III) preferably includes a binding molecule, phage, virus, nucleic acid and/or enzyme, especially it causes signal amplification by releasing further (III) from other vesicles. The vesicles and (III)-release system are brought into close proximity to (II) and/or (I), using a binding molecule, e.g. **antibody**, nucleic acid derivative, biotin, or generally any ligand.

USE - The method is useful in nucleic acid hybridisation and **antibody**/antigen assays, e.g. antenatal testing by fluorescent in situ hybridisation (FISH).

ADVANTAGE - The method is simpler than known processes since is does not require an enzyme and substrate, and (III) is present in active form. This allows a wider range of (III) to be used and may provide faster reaction rates, with generation of multiple (III) not dependent on the turnover rate of an enzyme.

Dwg.1/1

L17 ANSWER 3 OF 10 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1998:370209 SCISEARCH
THE GENUINE ARTICLE: ZM341
TITLE: Cloning and expression of rat lung acidic Ca2+-independent PLA(2) and its organ distribution
AUTHOR: Kim T S; Dodia C; Chen X; Hennigan B B; Jain M; Feinstein S I; Fisher A B (Reprint)
CORPORATE SOURCE: UNIV PENN, SCH MED, INST ENVIRONM MED, 1 JOHN MORGAN BLDG, 3620 HAMILTON WALK, PHILADELPHIA, PA 19104 (Reprint); UNIV PENN, SCH MED, INST ENVIRONM MED, PHILADELPHIA, PA 19104; UNIV DELAWARE, DEPT CHEM & BIOCHEM, NEWARK, DE 19716
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, (MAY 1998) Vol. 18, No. 5, pp. L750-L761.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 1040-0605.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 32

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A clone for a rat acidic Ca2+-independent phospholipase A(2) (aiPLA(2)) was isolated from a cDNA library prepared from rat granular pneumocytes with a probe based on the human aiPLA(2) sequence (T. S. Kim, C. S. Sundaresh, S. I. Feinstein, C. Dodia, W. R. Skach, M. K. Jain, T. Nagase, N. Seki, K. Ishikawa, N. Nomura, and A. B. Fisher. J. Biol. Chem. 272: 2542-2550, 1997). In addition,

a consensus sequence for mouse aiPLA(2) was constructed from several mouse cDNA clones in the GenBank and dbEST databases. Each sequence codes for a 224-amino acid protein with 88% identity of the amino acids among the three species and conservation of a putative **lipase** motif (GDSWG). Translation of mRNA produced from the rat clone in a wheat germ system resulted in expression of PLA(2) activity with properties similar to those of the human enzyme, i.e., acidic pH optimum and Ca2+ independence. The localization of aiPLA(2) in rat tissues was studied with the human cDNA probe, polyclonal and monoclonal **antibodies**, and aiPLA(2) activity. aiPLA(2) is present in the lung as evidenced by high levels of mRNA and protein expression and by enzymatic activity that is inhibited by anti-PLA(2) **antibody** and by the transition state analog 1-hexadecyl-3-trifluoroethylglycero-sn-2-phosphomethanol (MJ33). Immunocytochemistry showed the presence of aiPLA(2) in alveolar type II cells, alveolar macrophages, and bronchiolar epithelium. In the brain, heart, liver, kidney, spleen, and intestine, aiPLA(2) mRNA content was <50% of that in the lung, immunoreactive protein was not detectable, and enzymatic activity was not inhibited by MJ33 or aiPLA(2) **antibody**. These results show marked enrichment of aiPLA(2) in the lung compared with the other organs and suggest translational control of aiPLA(2) expression.

L17 ANSWER 4 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 94257687 MEDLINE
DOCUMENT NUMBER: 94257687
TITLE: Murine macrophages secrete factors that enhance uptake of non-lipoprotein [3H]cholesteryl ester by aortic smooth muscle cells.
AUTHOR: Stein O; Ben-Naim M; Dabach Y; Hollander G; Stein Y
CORPORATE SOURCE: Department of Experimental Medicine and Cancer Research, Hebrew University-Hadassah Medical School, Jerusalem, Israel..
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1994 Jun 2) 1212 (3) 305-10.
Journal code: A0W. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199409

AB We have recently demonstrated that macrophage conditioned medium (MP medium) and beta VLDL enhance cholesterol esterification in cultured aortic smooth muscle cells by LDL receptor mediated and other pathways (Stein, O. et al. (1993) Arteroscl. Thromb. 13, 1350-1358). In view of the presence of extracellular non-lipoprotein cholesteryl ester (in the form of lipid droplets) in the atheroma, the effect of MP medium on the cellular uptake of **liposomal** cholesteryl

linoleyl ether (CLE) or cholesteryl ester (CE) was studied. After 4 h incubation in MP medium, the uptake of **liposomal** [3H]CLE was up to 10-fold higher than in the presence of control medium of the same composition but not conditioned with macrophages (DV medium). Similar results were seen also with HSF derived from LDL receptor negative donors. The MP medium-stimulated uptake of **liposomal** [3H]CE resulted also in hydrolysis of 70-90% of the labeled compound, indicating that the [3H]CE was intracellular. While the MP medium effect on **liposomal** [3H]CLE uptake was evident after 4 h, its effect on [3H]cholesterol esterification by SMC in the presence of beta VLDL could be demonstrated only after 24 h. Addition of apoE to MP medium resulted in a small (30-40%) increase in the uptake of **liposomal** [3H]CLE; however, it was augmented more than 4-fold when apoE was added to DV medium. The MP medium effect on the uptake of **liposomal** [3H]CLE was interfered with by heparin, anti-LPL **antibody** or heparinase, while these treatments did not affect [3H]cholesterol esterification in the presence of beta VLDL. These results suggest that the interaction between SMC and two potential sources of lipids in atheroma, i.e., lipoproteins and non-lipoprotein lipid droplets, could be governed by different components of the MP medium. In the case of the lipid droplets, as modeled here in the form of **liposomes**, macrophage-derived lipoprotein **lipase** could play a major role in cholesteryl ester transfer into SMC.

L17 ANSWER 5 OF 10 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1993-036103 [04] WPIDS
CROSS REFERENCE: 1990-334588 [44]; 1993-093594 [11]
DOC. NO. NON-CPI: N1993-027698
DOC. NO. CPI: C1993-016327
TITLE: Treatment of diseases, e.g. AIDS, malignancy or diabetes - by site-specific instillaton or transformation of cells expressing therapeutic agent.
DERWENT CLASS: B04 B07 D16 P32 P34
INVENTOR(S): NABEL, E G; NABEL, G J
PATENT ASSIGNEE(S): (UNMI) UNIV MICHIGAN
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9300051	A1	19930107	(199304)*	EN	68
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE					
W: CA JP					
EP 591385	A1	19940413	(199415)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
EP 591408	A1	19940413	(199415)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					

US 5328470	A	19940712 (199427)	18
JP 06509328	W	19941020 (199501)	69
JP 06509329	W	19941020 (199501)	
EP 591385	A4	19961127 (199713)	
EP 591408	A4	19961127 (199713)	
US 5698531	A	19971216 (199805)	12
US 5707969	A	19980113 (199809)	12

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9300051	A1		WO 1992-US5242	19920626
EP 591385	A1		EP 1992-914172	19920626
			WO 1992-US5242	19920626
EP 591408	A1		EP 1992-914489	19920626
			WO 1992-US5243	19920626
US 5328470	A	CIP of	US 1989-331336	19890331
		CIP of	US 1991-724509	19910628
			US 1991-741244	19910726
JP 06509328	W		WO 1992-US5242	19920626
			JP 1993-501590	19920626
JP 06509329	W		WO 1992-US5243	19920626
			JP 1993-501591	19920626
EP 591385	A4		EP 1992-914172	
EP 591408	A4		EP 1992-914489	
US 5698531	A	CIP of	US 1989-331366	19890331
		Cont of	US 1991-724509	19910628
			US 1995-376522	19950123
US 5707969	A	CIP of	US 1989-331366	19890331
		Cont of	US 1991-724509	19910628
		Div ex	US 1995-376522	19950123
			US 1995-480320	19950607

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 591385	A1	Based on	WO 9300051
EP 591408	A1	Based on	WO 9300052
JP 06509328	W	Based on	WO 9300051
JP 06509329	W	Based on	WO 9300052

PRIORITY APPLN. INFO: US 1991-741244 19910726; US 1991-724509 19910628; US 1989-331336 19890331; US 1989-331366 19890331; US 1995-376522 19950123; US 1995-480320 19950607

AN 1993-036103 [04] WPIDS

CR 1990-334588 [44]; 1993-093594 [11]

Searcher : Shears 308-4994

AB WO 9300051 A UPAB: 19980202
Kit for treating a disease comprises a balloon catheter for insertion into a blood vessel carrying a means for delivery of a soln., and a soln. contg. an enzyme or mild detergent.

Also claimed are (1) a kit as above, where the soln. comprises at least 1 of hepanin, poly-L-lysine , polybrene, dextran sulphate, a polycationic substance and bivalent **antibodies**; (2) treating a disease in a patient by causing a cell on a vessel wall or in an organ or tissue to express an exogenous therapeutic agent protein to treat the disease; (3) treating a disease by site-specifically instilling or transforming cells, and (4) modulating the immune system of an animal by introducing into cells in vivo a recombinant gene, using a nucleic acid and a delivery vehicle or viral vector.

USE/ADVANTAGE - For site-specific admin. of a therapeutic agent, esp. dispase, trypsin, collagenase, papain, pepsin, chymotrypsim and **lipases**, to a blood vessel. Transformed cells are opt used invivo to express a therapeutic protein for the treatment of ischaemic disease, a vasomotor disease, diabetes, malignancy, AIDS, a genetic disease or a systemic disease. The animals immune system is opt. modulated to sensitise or tolerise the animal to a foreign molecule e.g, to reduce incidence of transplant rejection, or to stimulate the immunie system to protect against viral or microbial infection. Site-specific cell instillation can be used to replace damaged cells, or to introduce transformed cells.
Dwg.1/4

ABEQ US 5328470 A UPAB: 19940824
A medical treatment kit includes a balloon catheter insertable into and securable in a blood vessel, and a soln. of DNA and one or more of heparin, poly-L-lysine, polybrene, dextran sulphate, polycationic material or bivalent **antibodies**, optionally with a growth factor.

The soln. may contain dispase, trypsin, collagenase, papain, pepsin, chymotrypsin or **lipase**, Nonidet P-40, Triton X100, deoxycholate or Na dodecylsulphate, and a retrovirus, plasmid or **liposomal** formulation or a plasmid complex with a polycationic substance for transfer and uptake of RNA or DNA into a cell attached to a vessel, organ or tissue to cause it to express an exogenous therapeutic agent protein.

USE/ADVANTAGE - E.g. for treatment of tumour, cardiac disease or diabetes. Provides a novel method for site-specific administration of a therapeutic agent.
Dwg.0/4

ABEQ US 5698531 A UPAB: 19980202
Kit for treating a disease comprises a balloon catheter for insertion into a blood vessel carrying a means for delivery of a soln., and a soln. contg. an enzyme or mild detergent.

Also claimed are (1) a kit as above, where the soln. comprises at least 1 of hepanin, poly-L-lysine , polybrene, dextran sulphate,

a polycationic substance and bivalent **antibodies**; (2) treating a disease in a patient by causing a cell on a vessel wall or in an organ or tissue to express an exogenous therapeutic agent protein to treat the disease; (3) treating a disease by site-specifically instilling or transforming cells, and (4) modulating the immune system of an animal by introducing into cells in vivo a recombinant gene, using a nucleic acid and a delivery vehicle or viral vector.

USE/ADVANTAGE - For site-specific admin. of a therapeutic agent, esp. dispase, trypsin, collagenase, papain, pepsin, chymotrypsim and **lipases**, to a blood vessel. Transformed cells are opt used invivo to express a therapeutic protein for the treatment of ischaemic disease, a vasomotor disease, diabetes, malignancy, AIDS, a genetic disease or a systemic disease. The animals immune system is opt. modulated to sensitise or tolerise the animal to a foreign molecule e.g, to reduce incidence of transplant rejection, or to stimulate the immunie system to protect against viral or microbial infection. Site-specific cell instillation can be used to replace damaged cells, or to introduce transformed cells. Dwg.1/2

ABEQ US 5707969 A UPAB: 19980302

Kit for treating a disease comprises a balloon catheter for insertion into a blood vessel carrying a means for delivery of a soln., and a soln. contg. an enzyme or mild detergent.

Also claimed are (1) a kit as above, where the soln. comprises at least 1 of hepanin, poly-L-lysine , polybrene, dextran sulphate, a polycationic substance and bivalent **antibodies**; (2) treating a disease in a patient by causing a cell on a vessel wall or in an organ or tissue to express an exogenous therapeutic agent protein to treat the disease; (3) treating a disease by site-specifically instilling or transforming cells, and (4) modulating the immune system of an animal by introducing into cells in vivo a recombinant gene, using a nucleic acid and a delivery vehicle or viral vector.

USE/ADVANTAGE - For site-specific admin. of a therapeutic agent, esp. dispase, trypsin, collagenase, papain, pepsin, chymotrypsim and **lipases**, to a blood vessel. Transformed cells are opt used invivo to express a therapeutic protein for the treatment of ischaemic disease, a vasomotor disease, diabetes, malignancy, AIDS, a genetic disease or a systemic disease. The animals immune system is opt. modulated to sensitise or tolerise the animal to a foreign molecule e.g, to reduce incidence of transplant rejection, or to stimulate the immunie system to protect against viral or microbial infection. Site-specific cell instillation can be used to replace damaged cells, or to introduce transformed cells. Dwg.1/2

L17 ANSWER 6 OF 10 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 93:638841 SCISEARCH

THE GENUINE ARTICLE: MC444
TITLE: ENHANCED ANTITUMOR-ACTIVITY AND REDUCED TOXICITY OF 1,3-BIS(2-CHLOROETHYL)-1-NITROSOUREA ADMINISTERED IN LIPID MICROSPHERES TO TUMOR-BEARING MICE
AUTHOR: TAKENAGA M (Reprint); IGARASHI R; TSUJI H; MIZUSHIMA Y
CORPORATE SOURCE: ST MARIANNA MED UNIV, SCH MED, INST MED SCI, DIV DRUG DELIVERY SYST, 2-16-1 SUGAO, MIYAMAE KU, KAWASAKI 216, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (OCT 1993) Vol. 84, No. 10, pp. 1078-1085.
ISSN: 0910-5050.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 33
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Stable lipid microspheres (LM) and lipid nanospheres (LN) with average diameters of 200 nm and 50 nm, respectively, were used to encapsulate an lipophilic antitumor agent, 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU). LM and LN containing BCNU (lipo BCNU and s-lipo BCNU, respectively) were prepared by homogenizing a soybean oil solution of BCNU with egg yolk lecithin, and their antitumor activity via the intravenous route was tested against L1210 leukemia in mice and compared with that of BCNU dissolved in saline. Both lipo-BCNU and s-lipo BCNU showed significantly enhanced antitumor activity with reduced toxicity, when compared with the corresponding doses of BCNU alone. These results suggest that LM and LN may be suitable carriers for lipophilic antitumor agents and may enhance their efficacy.

L17 ANSWER 7 OF 10 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 92:599258 SCISEARCH
THE GENUINE ARTICLE: JR858
TITLE: CELL-SURFACE HEPARAN-SULFATE PROTEOGLYCANS FROM HUMAN VASCULAR ENDOTHELIAL-CELLS - CORE PROTEIN CHARACTERIZATION AND ANTITHROMBIN-III BINDING-PROPERTIES
AUTHOR: MERTENS G; CASSIMAN J J; VANDENBERGHE H; VERMYLEN J; DAVID G (Reprint)
CORPORATE SOURCE: CATHOLIC UNIV LEUVEN, CTR HUMAN GENET, CAMPUS GASTHUISBERG, O&N6, HERESTR 49, B-3000 LOUVAIN, BELGIUM; CATHOLIC UNIV LEUVEN, CTR THROMBOSIS & VASC RES, B-3000 LOUVAIN, BELGIUM
COUNTRY OF AUTHOR: BELGIUM
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (05 OCT 1992) Vol. 267, No. 28, pp. 20435-20443.
ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human aortic endothelial cells (HAEC) and human umbilical vein endothelial cells (HUVEC) were labeled with (SO42-)-S-35 for 48 h. The membrane-associated proteoglycans were solubilized from these monolayers with detergent and purified by ion-exchange chromatography on Mono Q, incorporation in **liposomes**, and gel filtration. The **liposome**-intercalated proteoglycans were I-125-iodinated and treated with heparitinase before SDS-polyacrylamide gel electrophoresis. Radiolabeled proteins with apparent molecular masses of 130, 60, 46, 35, and 30 kDa (HAEC) and 180, 130, 62, 43, and 35 kDa (HUVEC) were detected by autoradiography. Further characterization by affinity chromatography on immobilized monoclonal **antibodies** and by Northern blot analysis provided evidence for the expression of syndecan, glypican, and fibroglycan in human endothelial cells. Most of the heparan sulfate which accumulated in the subendothelial matrix was implanted on a 400-kDa core protein. This protein was immunologically related to perlecan and bound to fibronectin. Binding studies on immobilized antithrombin III suggested that all membrane-associated heparan sulfate proteoglycan forms had the capacity to bind to antithrombin III but that high affinity binding was more typical for glypican. Most of the proteoglycans isolated from the extracellular matrix also bound only with low affinity to antithrombin III. These results imply that glypican may specifically contribute to the antithrombotic properties of the vascular wall.

L17 ANSWER 8 OF 10 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92048591 EMBASE
DOCUMENT NUMBER: 1992048591
TITLE: In vitro glycation of human apoliprotein A(I) reduces its efficiency in lecithin:cholesterol acyltransferase activation.
AUTHOR: Gugliucci A.; Stahl A.J.C.
CORPORATE SOURCE: Laboratoire de Biochimie, Faculte de Pharmacie, Universite Louis Pasteur, B.P. 24,67401 Illkirch Cedex, France
SOURCE: Clinica Chimica Acta, (1991) 204/1-3 (37-42).
ISSN: 0009-8981 CODEN: CCATAR
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Non-enzymatic glycation of proteins occurs both in vitro and in vivo. This reaction may produce structural, immunological and

functional modifications of proteins which could contribute to the pathogenesis of the chronic complications of diabetes mellitus. Glycation of HDL apolipoproteins has been demonstrated using an antiglucitollysine monoclonal **antibody**. Low HDL-cholesterol levels associated with high VLDL and remnant levels is common in diabetic populations. This is probably a multifactorial phenomenon in which impairment of the function of both lipoprotein **lipase** [LPL] and lecithin:cholesterol acyltransferase (LCAT, EC 2.3.1.4.3) may be implicated. In fact, much of apolipoprotein A(I) (apo-A(I)) is transferred from VLDL to HDL particles. To test the hypothesis that glycation of apo-A(I) could reduce its ability to activate LCAT, we measured LCAT activity with both non-glycated and glycated apo-A(I) as activators, using **liposomes** containing [14C]cholesterol as substrate.

L17 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1977:234591 BIOSIS
DOCUMENT NUMBER: BA64:56955
TITLE: RELEASE OF PHOSPHO LIPIDS FROM **LIPOSOMAL** MODEL MEMBRANE DAMAGED BY **ANTIBODY** AND COMPLEMENT.
AUTHOR(S): KINOSHITA T; INOUE K; OKADA M; AKIYAMA Y
SOURCE: J IMMUNOL, (1977) 119 (1), 73-78.
CODEN: JOIMA3. ISSN: 0022-1767.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable
AB When **liposomal** membranes were attacked by **antibody** and [guinea pig] complement, enzymatic degradation of membrane phospholipids was not observed. Intact membrane phospholipids were released into the surrounding medium in amounts beyond that expected from nonspecific protein-phospholipid interaction. When **liposomal** membranes were treated with phospholipase A purified from venom of Habu snake (Trimeresurus flavoviridis), the trapped glucose marker was easily released, but phospholipids or their degradation products were not released into the medium and remained in the membrane structure.

L17 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1971:133301 BIOSIS
DOCUMENT NUMBER: BA52:43301
TITLE: FATE OF PHOSPHO LIPIDS IN **LIPOSOMAL** MODEL MEMBRANES DAMAGED BY **ANTIBODY** AND COMPLEMENT.
AUTHOR(S): INOUE K; KINSKY S C
SOURCE: BIOCHEMISTRY, (1970) 9 (24), 4767-4776.
CODEN: BICHAW. ISSN: 0006-2960.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable